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Table of Contents

The Edward Stirling Lectures.[1]

LECTURE II: ASCITES: THE ROLE OF THE LYMPHATICS IN THE ACCUMULATION OF ASCITIC FLUID.

By F. C. COURTICE,

Department of Experimental Pathology, The Australian National University, Canberra.

ASCITES is an accumulation of extracellular fluid in the peritoneal cavity. In healthy individuals there is little or no free fluid in the serous cavities, and the turnover of fluid and protein between the plasma and these cavities is small. In certain diseased states, however, which may be simulated in experimental animals, large volumes of fluid may grossly distend the peritoneal cavity, and the turnover rate of this fluid may be considerable (Courtice and Simmonds, 1954). As we shall see, ascites may be a localized accumulation of extracellular fluid, or it may form part of a generalized œdema. In either case, the total volume of extracellular fluid in a patient with ascites is greatly increased; the volume of ascitic fluid may be as much as the rest of the extracellular fluid in the body. This means that in the pathogenesis of this disorder large amounts of sodium and of water are retained. For every 120 to 140 mEq. of sodium retained, 1 litre of fluid accumulates.

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Mechanism of Sodium and Water Retention.

The mechanisms involved in this sodium and water retention have aroused much interest in recent years. In a normal individual the amounts of water and of sodium in the body are kept remarkably constant. The balance between intake and output is finely adjusted, largely by the action of two hormones, the antidiuretic hormone of the neurohypophysis (ADH) and the salt-retaining hormone of the adrenal cortex (aldosterone). These hormones by their action on the distal renal tubules of the kidney are responsible for determining the amount of water and of sodium reabsorbed. By their action the total amount of sodium, as well as its concentration in the extracellular fluid, is regulated within narrow limits.

The antidiuretic hormone is concerned with reabsorption of water, by which means the tonicity of the extracellular fluid is kept constant. The amount of ADH secreted by the neurohypophysis may be affected by many stimuli (Pickford, 1945), the most important of which are from osmoreceptors in the hypothalamus. These respond to changes in tonicity of the extracellular fluid (Verney, 1947). If the tonicity rises, more ADH is secreted, ensuring greater retention of water by the

renal tubules; if it falls, less ADH is secreted, so that more water is excreted in the urine. Whatever the total sodium content of the body, therefore, the antidiuretic hormone in general ensures a constant sodium concentration of the extracellular fluid.

With this mechanism functioning, the volume of extracellular fluid will depend upon the actual amount of sodium present, which is normally determined by the action of the salt-retaining hormone, aldosterone, on the renal tubules. If excess salt is ingested, the secretion of aldosterone is decreased; if salt in the diet is greatly restricted, aldosterone production increases. The mechanism regulating aldosterone production is, however, far from clear at present. There is probably a centre in the brain stem which regulates the secretion of aldosterone by the zona glomerulosa of the adrenal cortex, maybe by means of a humoral factor. Many different stimuli seem to affect this regulating centre (Farrell, 1958). The fact that the volume of extracellular fluid is determined by the amount of sodium present has led to the hypothesis that one of the most important stimuli to this centre is from volume receptors. The position of such volume or stretch receptors has not been determined, although several hypotheses have been put forward (Peters, 1952; Smith, 1957). Although the evidence for the position of such volume receptors is conflicting, it seems that stretch receptors somewhere in the vascular tree, probably atrium or veins, play an important role in regulating the amount of aldosterone secreted and therefore the amount of sodium in the body.

In this way, therefore, these two hormones are largely responsible in normal individuals for keeping both the concentration of sodium and the volume of extracellular fluid relatively constant. Any sodium ingested in excess of that excreted by the skin and the fæces passes out in the urine.

In a patient with ascites, however, most of the ingested sodium enters the peritoneal cavity and is retained, together with water (Farnsworth, 1948; Eisenmenger, 1952). Determinations of renal function show that in some cases there is a reduced glomerular filtration which plays some part in sodium retetion (Sims, 1950; Leslie, Johnson and Rolli, 1951). The main factor, however, in sodium retention is an increased reabsorption of sodium by the renal tubules brought about by an increased production or diminished degradation of aldosterone (Eisenmenger, 1952; Luetscher and Curtis, 1955; Axelrad, Cates, Johnson and Luetscher, 1955; Eisenmenger and Nickel, 1956). Greatly increased amounts of aldosterone and also of ADH (Rolli, Robson, Clark and Hoagland, 1945; Hall, Frame and Drill, 1949) are found in the urine, and experimental evidence suggests, although by no means conclusively, that this is due to an increased production of these hormones rather than to a decreased inactivation or breakdown by the liver. What we want to know is the cause of this increased production of the salt-retaining and antidiuretic hormones which has been observed, not only in ascites, but also in many other types of œdema such as nephrosis and congestive heart failure. The increased output of aldosterone runs parallel with periods of low urine sodium and accumulation of œdema. When improvement follows treatment of the underlying disease, the output of the hormone falls. Thus exacerbation of these diseases stimulates the secretion of aldosterone (Luetscher and Curtis, 1955).

It seems that the increased production of aldosterone is secondary to the formation of œdema and is not the primary cause. In most types of ascites, as we shall see, the primary cause is a fluid imbalance in the liver with the production of a greatly increased volume of tissue fluid, which spills over into the peritoneal cavity. This will lead to vascular collapse if sodium and water are not retained. The decreased effective plasma volume by way of the volume receptors causes an increased secretion of aldosterone and a retention of sodium. This will increase the sodium level in the plasma, but the action of the osmoreceptors, increasing the secretion of ADH, will retain water to compensate. These processes may be shown as follows:

Raised intrahepatic portal pressure
↓
Increased transudation in liver → ascites
↓
Decreased plasma volume
↓
Sodium retention
(volume receptors and aldosterone)
↓
Water retention
(osmoreceptors and ADH)

If this hypothesis is true, the effective plasma volume should be decreased in ascites. Total plasma volume varies somewhat in different individuals, and investigations show that there is no clear-cut evidence of a lower plasma volume in patients with ascites than in normal individuals. On the contrary, the total plasma volume may in some cases actually be increased. This may be due to the œsophageal varices and other dilated abdominal veins which accompany cirrhosis of the liver. It could be that, although the total plasma volume is increased, the effective plasma volume, or that part of the cardio-vascular system in which the volume receptors are situated, may be reduced. This is supported by the fact that in severe ascites there is peripheral vasoconstriction, and by the finding that when the anastomotic channels disappear after porta-caval shunt, the total plasma volume may drop to normal or below (Eisenberg, 1956). Until experiments have determined the exact anatomical situation of the volume receptors, this problem will remain unsolved.

Although some authors maintain that the primary factor in the formation of ascites is the renal retention of sodium (Habif, Randall and Soroff, 1953), the balance of evidence in the vast literature on this subject seems to suggest that the increased production of aldosterone and ADH are secondary to the prime cause of ascites, and that this mechanism is invoked to maintain the peripheral circulation and so prevent death from shock. In ascites, however, as in any type of œdema, the degree of œdema will be affected by the amount of sodium in the diet and also by the plasma protein level. Because of the primary fluid imbalance, ingested sodium more rapidly enters those tissues in which filtration is most favourable, that is, in the areas of œdema. In ascites, this is the peritoneal cavity. In the treatment of ascites, therefore, a rigidly reduced salt intake often reduces the amount of ascitic fluid (Eisenmenger, 1952; Habif, Randall and Soroff, 1953). The plasma proteins play an important role in preventing filtration across the capillary membrane. If the level of these in the plasma is low, as it often is in cirrhosis of the liver, filtration is increased and the degree of ascites may be accentuated. A diet rich in protein may help to restore the plasma albumin level and so reduce the extent of ascites (Patek, Post, Ratnoff, Mankin and Hillman, 1948; Habif, Randall and Soroff, 1953). But these factors are secondary or subsidiary to the primary cause of ascites.

Clinical and Experimental Ascites.

Let us first consider briefly the clinical conditions which may be associated with ascites and the ways in which these conditions have been simulated in experimental animals.

In man ascites is most commonly associated with a rise in intrahepatic portal pressure, seen in Laennec's cirrhosis of the liver, in congestive heart failure, in constrictive pericarditis, and in the rare cases of thrombosis of the hepatic veins (Chiari's syndrome). In animals these diseases have been simulated and ascites has been produced: cirrhosis of the liver has been produced by a variety of substances such as chloroform and carbon tetrachloride, or by a choline-deficient diet, while the changes in congestive heart failure, constrictive pericarditis or Chiari's syndrome have been produced by

valvular incompetence or by constricting the inferior vena cava between the liver and diaphragm (Hyatt and Smith, 1954).

Extrahepatic portal hypertension alone does not produce ascites to any degree, either in man or in experimental animals. Thrombosis of the portal vein without liver disease leads to extrahepatic portal hypertension with extensive collateral circulation (through œsophageal varices, umbilical veins and hæmorrhoidal veins), but without ascites (Davidson, 1954; Child, 1955; Eisenmenger and Nickel, 1956). In animals, too, the portal vein has been partially constricted, leading to congestion of the spleen and alimentary tract, but with only transient ascites (Volwiler, Grindlay and Bollman, 1950; Schilling, McCoord, Clausen, Troup and McKee, 1952; Lake, 1955).

Ascites may also be evident in other clinical states in which the liver and the portal circulation are normal. In severe hypoalbuminæmia occurring in the nephrotic syndrome or in malnutrition, ascites is part of a generalized œdema resulting mainly from the very low albumin level in the plasma. A similar condition may be produced in animals by plasmaphoresis, by lesions simulating the nephrotic lesion and by protein deprivation. Localized lesions of the peritoneum will also give rise to an accumulation of fluid in the peritoneal cavity, as in carcionomatosis peritonei, tuberculous peritonitis and Meigs's syndrome. In these conditions the ascitic fluid is derived from the vessels in the peritoneum.

A different type of ascites may be produced by blockage or rupture of the thoracic duct in the peritoneal cavity. Here the chyle, instead of being transported to the bloodstream, pours into the peritoneal cavity and a chylous ascites results.

Of all these different types of ascites, the first group in which there is a raised intrahepatic portal pressure is the most common and has attracted a great deal of attention from all branches of our profession—the physiologist, the pathologist, the physician and the surgeon. In addition to our own profession, cirrhosis of the liver has attracted attention from other groups of people because of the rising incidence of chronic alcoholism in several countries. The mode of action of alcohol in alcoholic cirrhosis has for many years been the subject of controversy amongst medical scientists, and chronic alcoholism has become a considerable social problem. Today, however, we are interested only in one aspect of cirrhosis of the liver, the disturbance of fluid balance which leads to ascites. There are many people with some degree of cirrhosis of the liver who show no symptoms; we have all seen an unsuspected cirrhotic liver at post-mortem examination when death has been due to some other cause.

The Portal Circulation.

Before considering the mechanisms primarily concerned in the formation of ascitic fluid, we should mention briefly the hæmodynamics of the portal circulation. At rest the total blood flow through the liver of an adult man is 1250 to 1500 ml. per minute, or about 25% of the cardiac output. The bulk of this blood is supplied by the portal vein: in dogs about 80% comes from the portal vein, a low pressure system, and 20% from the hepatic artery, a high pressure system, and both sources of blood mix in the sinusoids. The proportions of blood, and therefore of oxygen, derived from these two sources probably vary considerably in different animals and in different conditions, and are not easy to determine accurately (Popper and Schaffner, 1957).

The blood flow through the liver is complex. Between the aorta and portal vein are several circuits in parallel including the splenic, gastric, pancreatic, mesenteric and colic arteries (Figure I). All these circuits form a variable resistance to flow between the aorta, in which the systolic pressure is 140 mm. of mercury, and the portal vein, in which the pressure is usually about 10 mm. of mercury or less. This splanchnic resistance may vary from time to time, and so the pressure and flow in the portal vein will be affected (Bradley, 1958). There is another resistance at the level of the portal venules, before the blood mixes in the sinusoids with blood entering the liver by way of the hepatic artery. The arterioles of the hepatic artery offer a variable resistance to the blood flow from this source and thus also affect the flow and pressure in the sinusoids. There are thus several pre-sinusodial resistances to the blood flow from the aorta to the hepatic sinusoids. In addition, the blood must traverse a post-sinusoidal resistance, the venules of the hepatic veins, before entering the inferior vena cava. The flow and pressure within the hepatic

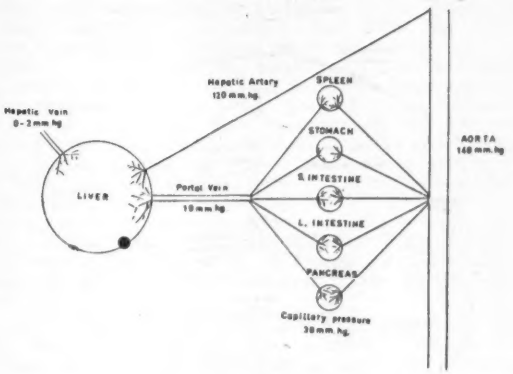

FIGURE I.
Diagrammatic representation of the portal circulation.

sinusoids may thus be affected by a number of mechanisms.

Ascites is an accumulation of extracellular fluid, and must therefore be due to some abnormality in the mechanisms which control the balance between plasma on the one hand and the tissue fluid on the other. In maintaining this balance, the lymphatics normally play an important role in most tissues of the body. Associated with the portal circulation there are rich lymphatic plexuses which are capable of transporting very large volumes of tissue fluid. There are what we call "tissue fluid pools" drained by groups of lymphatics, and, broadly, these are three in number (Figure II). The gastro-intestinal tract forms the first. Here, considerable fluid exchanges occur between the circulating plasma and the tissue fluid on the one hand and the lumen of the gut and the tissue fluid on the other. In this way, this tissue fluid pool differs from others. The lymphatics of the gastro-intestinal tract not only are responsible for the absorption of fat from the lumen, but normally return large quantities of tissue fluid and plasma protein to the blood-stream. The second pool is in the liver and is drained by a dense network of lymphatic capillaries in the periphery of the lobules to the hepatic lymph ducts. The third pool is the free fluid in the peritoneal cavity, which is drained by the lymphatics of the peritoneum, mainly by the lymphatics of the diaphragm.

A great deal has been written about ascites and the many variable factors which may cause ascitic fluid to form intermittently. No doubt many factors, some of which I have already mentioned, affect the accumulation of fluid in the peritoneal cavity. Today, I should like to stress the magnitude of the role of the lymphatic vessels in keeping the peritoneal cavity free from fluid. The volumes of lymph which the three groups of lymphatics are capable of carrying are large. Normally the lymph flow from the hepatic and intestinal ducts accounts for probably 90% of the total lymph flow of the body, which in man is 2 to 3 litres per day, that is, approximately equal to the plasma volume (Yoffey and Courtice, 1956). The plasma circulates within the

vascular system many times a day, at least once a minute, and during this time some of the plasma is filtered to form tissue fluid, of which the lymphatics return 2 to 3 litres per day. The main function of the lymphatics is to return to the blood-stream the plasma proteins that have escaped from the circulation. By far the greater part of the escaping protein, and in the course of a day about 50% to 100% of the intravascular plasma proteins escape, is returned by the hepatic and intestinal ducts (Figure III). It can be understood,

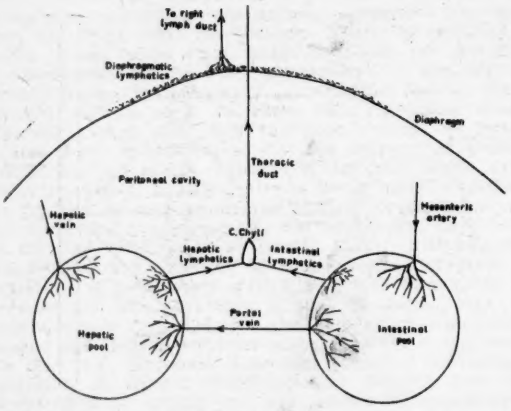

FIGURE II.
Diagrammatic representation of the tissue fluid "pools" and lymphatics associated with the portal circulation.

therefore, what an important role these lymphatics play in the normal fluid exhanges in these tissues; but in certain circumstances their lymph flow may increase ten-fold or more. This would mean, as we shall see, that they can return to the blood-stream 20 litres or more of tissue fluid per day.

The lymph flow from the diaphragmatic lymphatics through ducts traversing the anterior mediastinum to enter mainly the right lymph duct is probably very

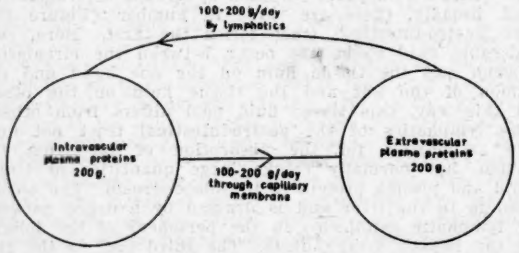

FIGURE III.
Extravascular circulation of plasma protein.

small in normal circumstances. In ascites, however, this flow can be considerable: a volume equal to the entire plasma volume has been absorbed during the course of a day from the peritoneal cavity of experimental animals, though the proportion in man is somewhat smaller (Courtice and Simmonds, 1954). I mention these figures here to stress at the outset that the function of the lymphatic vessels in these regions is by no means insignificant in the exchanges of fluid and protein that take place in health or in disease. There may occur between the circulating plasma and the extravascular or tissue fluid large fluid shifts, which are removed by the lymphatics without producing œdema.

Exchange between Circulating Plasma and the Tissue Fluid Pools of the Gastro-Intestinal Tract and of the Liver.

The exchange of fluid in the gastro-intestinal tract, especially in the small intestine, may be considerable. During digestion large volumes of fluids are exchanged through the mucosa in both directions, depending largely on osmotic gradients and pressures. At the same time fluids are exchanged through the blood capillary membrane, depending upon the blood flow and the balance of pressures existing at the time. The rich lymphatic network drains away excess tissue fluid, and the lymph flow is affected by the formation of tissue fluid, the tissue pressure and the movements of the gut wall. The fluid exchanges in this region are, therefore, complex. When a large volume of fluid is ingested, it passes through the intestinal mucosa into the tissue fluid, and there it will be absorbed largely by the blood vessels, but to quite an appreciable extent also by the lymphatics. When filtration through the blood capillaries is increased, the filtrate enters the tissue fluid pool and may be removed by the lymphatics or pass through the mucosa into the lumen of the gut. The lymphatics of the gut play a very prominent role in these fluid exchanges, in order to prevent any excessive increase in the size of the tissue fluid pool or œdema. Normally, in an adult man, they return to the blood-stream one to two litres of tissue fluid a day, and are capable in emergency of increasing this flow tenfold (Yoffey and Courtice, 1956).

The fluid exchange in the liver occurs between the blood in the sinusoids and the tissue fluid in Dissé's space, and the liver lymphatics drain away any excess. Much controversy has arisen concerning the histological structure of the liver sinusoids. It was fairly generally believed that the liver cells were separated from the blood in the sinusoids by an extremely delicate and probably very permeable membrane. The beautiful pictures of this sinusoidal membrane obtained by electron microscopy by Bennett and his colleagues (1958) have certainly clarified to some extent our conception of the exchange in the liver. Bennett has shown that there are large gaps, some several thousand Ångström units in diameter, in the sinusoidal membrane, and that through these gaps the plasma and the plasma proteins freely communicate with the Dissé space. It would seem that, depending on pressure gradients, the fluid in the Dissé space, which is almost the same as plasma, may reenter the sinusoid or pass to the periphery of the lobule to enter the lymphatics which form a rich plexus surrounding the lobules. Lymph that enters these lymphatics is drained away by the hepatic lymph duct, which joins with the intestinal vessels in contributing most of the lymph to the thoracic duct.

The lymph flow from the liver is normally very high, but somewhat less than that from the intestines. In dogs (Nix, Mann, Bollman, Grindlay and Flock, 1951; Ritchie, Grindlay and Bollman, 1959) the lymph flow is about one-third to one-half the thoracic duct flow, while in cats the liver contributes about one-third of the thoracic duct flow (Morris, 1956). If in man the process occurs in a similar manner, approximately one litre of hepatic lymph will be formed per day.

The protein content of the liver lymph is always very high, usually up to 90% or more of the plasma levels, whereas intestinal lymph proteins are usually about 50% to 60% of the levels found in the plasma. In the liver, therefore, in spite of a very low sinusoidal pressure, about 10 mm. of mercury, the delicate sinusoidal membrane in which there are large gaps is responsible for a high production of lymph rich in plasma protein. In the gastro-intestinal tract the capillary pressure is much higher, about 30 mm. of mercury, but the capillary membrane is less permeable, so that the lymph flow is high, but the lymph contains less protein.

That most of the protein in the liver lymph comes from the plasma has been shown by labelling the intravascular plasma proteins either with I^{131} or with the blue dye T1824. In such experiments the specific activity

of the hepatic lymph approaches that of the plasma much more rapidly than in the case of the intestinal lymph. In the liver there is a small extravascular pool of fluid and protein with a high turnover rate, so that the specific activity of the hepatic lymph reaches that of the plasma normally in about two hours. In the intestines we have a large extravascular protein pool with a large turnover, but not so rapid as in the liver (Morris, 1956).

In considering the factors concerned in the production of ascites, the fluid balance in these two regions is of considerable importance. A large volume of blood normally flows through the blood vessels of the gastro-intestinal tract and the liver, and the filtration through the capillaries is relatively high. Should any imbalance of the forces controlling the exchange of fluids across the capillary membrane occur, a great increase in tissue-fluid formation will result. If this is not removed by the lymphatics, the tissues will become œdematous. Experiments have therefore been devised in which the hæmodynamics of the portal circulation have been altered in various ways, and the effects on the lymph flow and the formation of ascites observed.

Effect of Increasing Extrahepatic Portal Pressure by Partial Occlusion of the Portal Vein or Portal Vein Thrombosis.

If its portal vein is suddenly occluded, an animal will die of circulatory collapse or shock, because the greater part of the circulating blood will stagnate in the congested splanchnic vessels. If, however, the portal vein is only partially occluded, this will lead to extrahepatic portal hypertension with raised capillary pressure in the gastro-intestinal tract. This will further lead to greatly increased filtration through the splanchnic vessels into the wall of the alimentary tract. The excess tissue fluid formed results in great increase in the lymph flow from the thoracic duct, as was shown by Starling in 1894, and a transudation of fluid into the lumen of the gut (Verzar and McDougall, 1936), but only a transient and moderate ascites (Volwiler, Grindlay and Bollman, 1950; Schilling *et alii*, 1952; Lake, 1955). It would seem, therefore, that no matter how great the filtration of plasma into the gut wall, very little tissue fluid passes through the peritoneum into the peritoneal cavity. This may be due partly to the ability of the lymphatic vessels to remove large volumes of tissue fluid, and partly to the fact that the rich capillary plexuses, through which filtration is increased, are closer to the lumen of the gut. Any rise in tissue fluid production and pressure would force the fluid either into the lymphatics or into the gut lumen.

Effect of Overloading the Circulation with Large Doses of Ringer-Locke Solution on Fluid Exchange in the Liver and Intestines.

Another way of greatly increasing the filtration through the capillaries of the gastro-intestinal tract is to give large intravenous infusions of isotonic Ringer-Locke solution. The greater part of the infused fluid rapidly leaves the circulation in the high-pressure regions. In our experiments, in which continuous infusions have been given over a period of five hours, about half the fluid passes out in the urine and the rest enters the extra-vascular compartment of the tissues, but extremely little appears in the serous cavities even when massive infusions are given (Courtice, Harding and Korner, 1954).

In these circumstances, the lymph flow from the intestinal lymph ducts rose ten-fold to fifteen-fold, whereas that from the hepatic duct increased but little. The turnover of protein in the tissues drained by the intestinal duct was also very greatly increased, whereas that in the liver was much the same as normal. These experiments again show that, when filtration through the capillaries of the gastro-intestinal tract is greatly increased, the lymph flow increases many times, but little or no free fluid accumulates in the peritoneal cavity. It would seem from these experiments, therefore, that extrahepatic portal hypertension may very greatly increase the formation of tissue fluid in the gut; but provided the musculature of the gut wall is functioning normally, very little of this tissue fluid enters the peritoneal cavities.

Effect of Increasing Intrahepatic Portal Pressure by Partial Occlusion of the Inferior Vena Cava between Liver and Diaphragm and by Inducing Cirrhosis of the Liver.

In contrast to these experiments, an increase of portal pressure within the liver sinusoids will give rise to ascites. Many investigators have partially occluded the inferior vena cava between the liver and the diaphragm, in this way raising the intrahepatic portal pressure. In these experiments the lymph flow from the liver increases enormously, whereas that from the gastro-intestinal tract increases only slightly. If this increased formation of lymph is maintained in chronic experiments, ascites will result. The liver lymphatics are grossly dilated, and the lymph flow continues at the greatly increased level (Nix, Mann, Bollman, Grindlay and Flock, 1951). Similar results have been obtained in rats and dogs with cirrhosis of the liver induced by repeated administration of carbon tetrachloride (Nix, Flock and Bollman, 1951). In these circumstances, the intrahepatic portal pressure is raised, probably because of a reduction in the hepatic venous system; this restricts the outflow through the hepatic veins (Madden, Lore, Gerold and Ravid, 1954).

In man there have been no direct measurements of lymph flow from the liver. The lymphatic vessels at the hilus, however, are increased in size and number when ascites is caused by cirrhosis of the liver or congestive heart failure, but not in ascites due to neoplastic involvement of the peritoneum (Baggenstoss and Cain, 1957). It would seem, therefore, that in man, as in experimental animals, the hepatic lymph flow is several times increased in cirrhosis of the liver and congestive heart failure.

These experiments suggest that the ascitic fluid in these circumstances comes from the spill-over of extracellular fluid from the liver when the lymphatics can no longer deal with the rate of production of tissue fluid. Whereas any excess tissue fluid in the gut wall not removed by the lymphatics usually passes into the lumen of the gut, in the liver such an excess passes into the peritoneal cavity. However, it must be emphasized that in a normal individual the liver lymphatics probably return a litre of tissue fluid per day to the blood-stream, and can return several times this amount without loss to the peritoneal cavity. So long as the liver lymphatics can cope with this increased load, ascites does not occur, and the salt and water retaining mechanisms are not invoked. When, however, the fluid balance in the liver is such that the lymphatics can no longer compensate, fluid in large quantities may spill over into the peritoneal cavity, reduce the effective plasma volume and set in motion the processes leading to salt and water retention.

The Removal of Peritoneal Fluid.

Once the limit of the capacity of the liver lymphatics is reached, therefore, free fluid will enter the peritoneal cavity. Ascites will result in these circumstances only when this spill-over is so great that the removal mechanisms cannot cope. As we have mentioned earlier, the lymphatics in the diaphragm are capable of removing in man a considerable amount of fluid, probably a litre or more per day. Ascitic fluid is isotonic and contains a considerable amount of protein, the level of which varies in different conditions, being lowest in cirrhosis of the liver and highest in carcinomatosis or peritonitis. Any plasma protein introduced into the peritoneal cavity is removed only by the lymphatics and this almost entirely by the lymphatics of the diaphragm (Courtice and Simmonds, 1954). These drain into large collecting ducts, which run with the internal mammary vessels on either side of the sternum to reach the anterior mediastinal lymphatic nodes in the region of the thymus. From these nodes efferent lymphatic vessels pass, as a

rule, to the right side to join the right lymph duct, but sometimes the efferents may pass to the left side. This lymphatic route through the anterior mediastinum accounts for about 80% of the lymph from the diaphragm. Subsidiary routes account for the rest.

It was once thought that absorption of protein solutions from the peritoneal cavity was very slow (Cunningham, 1926). If we compare the rate with that of hypotonic salt solutions it is slow, for in these circumstances water very rapidly diffuses into the blood vessels of the peritoneum until isotonicity is reached. Protein-rich plasma, however, is removed as rapidly as isotonic sodium chloride or Ringer-Locke solution. In unanæsthetized experimental animals, 20 ml. per kilogram—that is, about half the plasma volume—is removed within five hours in the rat, eight hours in the rabbit and 16 hours in the guinea-pig. In larger animals and in man this rate is slower, but it is still fairly rapid.

Not only can protein molecules readily pass through the peritoneum covering the diaphragm, but particles up to the size of red cells are also readily absorbed by this route (Courtice, Harding and Steinbeck, 1953). Absorption from the peritoneal cavity is aided by the movements and changes in pressure associated with respiration, particularly with the excursions of the diaphragm. Anæsthesia or paralysis of the diaphragm slows absorption, while increased respiratory movements increase absorption (Morris, 1953). Evidence suggests that the protein molecules and particles pass between the mesothelial and lymphatic endothelial cells, and that their passage is greatly aided by the rhythmic stretching and relaxing of these structures overlying the diaphragm. It also seems that the basement membrane in this region is very scanty, so that this does not impede the passage of materials into the lymphatics once the mesothelium has been passed. In other parts of the peritoneal cavity there is a dense basement membrane beneath the mesothelium. As we have already seen with blood capillaries, the density of the basement membrane seems to play an important role in the passage of materials.

These experiments give an indication of the functional significance of the diaphragmatic lymphatics in keeping the peritoneal cavity free of fluid. Normally, the lymph flow in these lymphatics is very small, which suggests that it is only in exceptional circumstances, such as the production of ascites, that they function to their full capacity. It is interesting that a mechanism with such a large reserve of function should develop, when this reserve is perhaps never called upon in the vast majority of individuals.

In ascites this reserve of function ensures a very rapid turnover of protein—out through the liver sinusoids, spilling over into the peritoneal cavity, through the liver capsule and returning to the blood-stream by way of the diaphragmatic lymphatics. McKee, Whipple and their co-workers found that the exchange between plasma and ascitic fluid of C^{14}-labelled plasma proteins was very high in dogs actively forming ascitic fluid after constriction of the inferior vena cava above the liver: about 6% of the circulating albumin passed each hour from the blood-stream to the ascitic fluid, to be returned by the diaphragmatic lymphatics.

We see, therefore, that in the shifts of fluid which take place when ascites develops, three major sets of lymphatics are involved—the lymphatics of the alimentary tract, the liver lymphatics and the lymphatics of the diaphragm. All these are capable of carrying large volumes of lymph. It is, therefore, only in extreme circumstances and in the presence of severe disease that gross ascites becomes evident.

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THE ASTHMATIC SEIZURE: ITS MECHANISM AND MANAGEMENT.[1]

By GERALD DOYLE,
Melbourne.

THE problem of relieving an asthmatic seizure is one which may confront a medical man at any time. In practice, however, the physician uses regular therapeutic measures. These arise frequently from clinical deductions influenced by the patient's likes and dislikes. Observations made by patients concerning their illnesses are accepted by medical men, but their accuracy is rarely checked.

The methods used by the medical profession should vary according to whether the patient is an old chronic sufferer, an occasional asthmatic, or a new asthmatic. This last class can be divided into those who have had previous attacks undiagnosed or untreated by a medical man, and those in whom the physician has had the opportunity of observing the first attack.

In most cases, by the time the seizure has advanced to the stage where medical help is required, the patient is too breathless and exhausted to give a correct history. The physician is then dependent on the observations of the patient's relatives.

The obtaining of an accurate history from a patient experiencing relief from an asthmatic attack after treatment with one of the sympathomimetic drugs is impossible, because of the profound psychological effect on most patients. The safest procedure is to make sure that the patient is suffering from true asthma, afford him relief, and wait until the next day before questioning him.

Information sought from the relatives should include how long the attack has been in progress, and the presence of any signs and symptoms, physical and psychological, indicating that an attack was about to begin within an hour or so. Those preceding the wheezing or indicating any change in the type of breathing are of great importance. Some patients can anticipate an attack by observing the presence of a bump or a snatch in the course of inspiration. These observations occur in inspiration, and precede the difficulty noted later on expiration so characteristic of the disease. Few incorrect observations are made concerning wheezing.

Spasm is generally felt in the region of the diaphragm and can easily be mistaken for pain. The medical attendant must make sure that he is dealing with an asthmatic seizure and not with one of the conditions imitating it. To clarify any difficulties, the following outline of an attack is submitted.

Asthma has a cycle of signs and symptoms, consisting of an attack followed by a period of freedom, and completed by the appearance of another attack. Though asthma is periodic, one notes that, though there is a period for each case, there is none for the disease in general.

The attack can be described in three stages. These can be demonstrated in any asthmatic in any attack. The stages are definite and distinct, one being dominant, and as in all allergic phenomena, this is not always the same stage. In addition, one symptom is always outstanding. It is generally the same symptom in the same stage for a particular asthmatic, although this is not always so. One stage and one symptom being dominant, asthma will persist in this manner for a series of attacks. If there is a long enough interval between attacks, a change may take place. There is a large number of combinations of stage and symptoms, according to which stage and which symptom are dominant.

When an asthmatic affirms that his case is different from other cases, I believe him. After seeing many asthmatics, one falls into the habit of typing them. A clearer understanding and better treatment result. Consideration of these types shows the following three.

1. Type I with Stage I dominant. Nervous symptoms are outstanding, wheezing and spasm minimal, and the third stage is noted only because of the occasional presence of a cough. It is very suitable for therapeusis by sedative and mild stimulo-expectorant drugs. Only rarely is it necessary to use the sympathomimetic variety. This is the closest approach to a true nervous asthma.

2. Type II with Stage II dominant. This is the true standard spasmodic type of asthma, a description of which is unnecessary.

3. Type III with Stage III dominant. In this type the early stage is barely noticed, the second stage is present but not severe, while the third or major stage is unduly prolonged. The sputum is copious and mucopurulent, and, generally, the condition resembles bronchitis. Relief is brought about by orally administered drugs.

The variable factor in all types is the resting phase, this being constant in appearance to within an hour. In other words, the patient with established asthma knows about when to expect his attack. Certain agents mentioned later can upset the cycle, but the basic cause of the asthma is still present. The agents are the cause but the cause may not be the same in each case.

This resting phase can be altered by the patient by disobeying the rules. An asthmatic knows well the necessity for rules and what happens when they are broken. Some agencies shorten the resting phase, while a few prolong it. The main agent in producing an attack is disobedience in the matter of diet, exercise and temperament. Conditions tending to raise bodily tension, especially those associated with the primary emotions of fear, hatred, love and anger, are next in importance.

Atmospheric changes are powerful agents. Cold winds and frosty nights will alter the cycle and produce an attack before the usual time. An incomplete second stage will also shorten this phase. Unusual and unexpected contact with offending allergens can bring about the same result. With some agents, such as food and pollens, the chain of cause and result is easy to follow. The time interval is usually short and within the memory of the patient. In the case of allergens, this is not always so. For example, an asthmatic is known to have had contact with a certain recognizable dust to which he is known to be sensitive. In the normal course of events he will expect an attack, either soon after the exposure or at least during the same night. When this happens, both patient and physician agree as to cause and effect. The presence of the recognizable dust in the sputum clinches the diagnosis. If there was no sputum, the diagnosis would by no means be certain. If dust was found on the two following nights, the diagnosis would be doubted. But when the patient has developed a degree of immunity, dust may not appear until the third night, although present from the first night. The dust, when seen, will be found in clumps on the large airless lumps of sputum, as if the cilia in the tubes were trying to sweep the dust ready for expectoration. It takes the lung at least three days to get rid of an allergen once inhaled. This observation indicates how difficult it can be to associate an attack of asthma positively with a definite allergen.

Conditions intensifying an infection present beforehand, such as over-exertion, working in a cold wind or inhaling

[1] Read at a meeting of the Victorian Branch of the Australian Society for the Study of Allergic Diseases in August, 1957.

an irritant gas, achieve a similar result. Any condition lowering the allergic threshold can also break the cycle. Each asthmatic has a special personal clause for inclusion in this section, and begins this part of his history with the words "whenever such-and-such happens".

STAGE I.

The patient may not be aware that certain symptoms or sensations are the forerunners of an attack. If the physician takes the trouble to make the necessary explanations, it will not be long before the patient can foretell his attacks hours before he would have been able to do so in the normal course of events. The following are the usual symptoms, which can appear in any order: (i) tiredness leading to extreme weariness; (ii) mental irritability; (iii) a sense of oppression in the chest; (iv) marked consciousness of the respiratory act.

Some asthmatics are troubled with extreme weariness and uncontrollable drowsiness leading to a deep sleep an hour prior to an attack. They are wide awake, however, when the attack begins. Nervous symptoms are very marked in children, and overshadow the fact that Stage II, which follows, is the real disease. Many physicians, not realizing that this is only a stage in the disease, think that it is the cause of Stage II. This has led to much misunderstanding. The final symptom in Stage I is "heavy breathing". This always precedes the second stage. In some asthmatics, heavy breathing ushers in the second stage and reappears after relief begins and before it is complete. Thus it ushers the attack in and out.

At the beginning of this stage, breathing exercises and psychotherapy may help. Their success depends on the ability of the patient to relax his muscles completely and to free his mind from the usual and unusual worries of existence. This is impossible for an asthmatic in the early stages of a spasm. If the patient can relax enough to cough up some sputum, the attack may pass off. Much depends on just how far the attack had progressed before the treatment was commenced. Some asthmatics can delay the attack by slow breathing. With practice it is not difficult to slow the respiratory rate to six or even four respirations to the minute. The principle is the same as the one used by the golfer who practises slow swings with the club to iron out a snatch in his swing. The rationale is to relax the muscles, loosen the sputum, and so free the airway. Once wheezing has commenced and spasm set in, all these remedies are merely a waste of time.

STAGE II.

The second stage begins with the appearance of either spasm or wheezing. Prior to this point the precipitating agents appear as a minor symptom, as a cough or as tickling of the throat by air-borne particles in a smoke-laden room. Unexplained irritated areas can arise in the pharynx and lead to coughing and pharyngeal discomfort while the patient is eating. This is a very common way for an attack to be precipitated. Gastric distension, pyloric spasm, or intestinal irritation or distension can be just as effective in bringing a spasm to life, by preventing proper descent of the diaphragm. It seems that any of the widely spread branches of the vagus nerve have the power to act as a focus. This explains the bizarre stories related by patients to the physician of how their particular brand of asthma begins. Patients aware of this danger period are chary of taking food in the heavy-breathing stage. Some physicians prescribe for asthmatics under their care a small dose of adrenaline about twenty minutes before meals. In this way the patient can eat his meal in peace. If the precipitating agents are not present to precipitate the attack, this will appear later. The time of appearance is influenced by factors at present unknown.

There are five main symptoms in the second stage. It begins with the appearance of spasm and finishes when the spasm is over. One must remember that wheezing is not spasm and vice versa. They are independent symptoms and signs, and can occur together or apart. The five main symptoms are: (i) bronchial spasm, (ii) wheezing, (iii) cough, (iv) dyspnœa, (v) pain. As in all allergic diseases, any one of these five features can be the major one. This accords the physician many variations in the clinical picture.

Spasm is unpredictable in its action and in its intensity. It is established among asthmatics, if not among members of the medical profession, that there is no way of knowing in advance whether the spasm will be gentle or severe in its approach. It can switch the patient from Stage I to Stage II in a fraction of a second. Generally, the swift and violent spasms are seen in patients taking very large doses of adrenaline over a period of time, and after the inhalation of violently irritating gases. They can also follow an incompletely relieved second stage due to an underdose of adrenaline, and are due to the reactionary effect of adrenaline.

The area of the bronchial tree affected by spasm is a subject of conjecture. It seems that more or less the same process goes on here as in the nose. The mucous membrane of each is different in some respects, but they are both part of the respiratory mechanism and both are subject to the same allergens. If the physician inspected the nasal passages of every asthmatic, with or without nasal symptoms, he would notice that a high percentage of asthmatics have nasal allergic signs. These may be noted on one side only, or equally on both sides, or major manifestations may occur on one side and minor on the other.

Generally, chronic asthmatics carry in their nose some sign or other of allergy. If this idea was applied to the lung, it would explain the statements of patients that the asthma is present on one side or that one side is worse than the other, or that both sides are equally affected. Our knowledge of the disease does not allow us to interpret these statements correctly.

The nearer the spasm is to the alveolus, the more severe, silent and dangerous it is. Mid-bronchial spasm, on the other hand, is noisy and not dangerous. The farther away from the patient that the physician can hear the wheezing, the less the danger to the patient. When the spasm is in the area of the bronchial tree where the bronchial rings are incomplete, there is danger. Spasm in this area can take the form of pain. The pain is often regarded as cardiac and not pulmonary in origin, the dyspnœa being so intense that the patient forgets the pain.

Severe pain is common in patients at the height of status asthmaticus, when the violence of the spasms is at its peak. The spasms occur in quick succession after attempts at relief. With deep-seated spasms, it is usual to have minimal or absent wheezing. Dyspnœa is the outstanding symptom and sign of this stage. It can be very intense, leading the patient to think that he will choke and die. To him the seconds are minutes and the minutes hours.

On examination, the physician will notice that there is inspiratory retraction in the supraclavicular areas and also in the suprasternal notch, coupled with retraction in the areas of the diaphragmatic attachment. It is absent or minimal caudal to the costal margin. This agrees with the radiographic observation of practically no descent of the diaphragm during an asthmatic spasm.

The attacks follow the clinical rule—wherever in the respiratory tract there is an obstruction, there also is movement. In asthma the larynx is still, but the chest, both in the region of the diaphragm and above, moves in violent agitation. Asthmatic dyspnœa has been always spoken of as an expiratory variety, but asthmatics will agree that inspiration is more vital than expiration. When relief comes, inspiration brings it.

In the earliest phases of an attack located in the mid-bronchi, the usual location, inspiration is longer than expiration. As the attack proceeds, they are almost equal, and then expiration becomes longer than inspiration, as before mentioned, but it is inspiration which gives relief. The higher in the bronchial tree the spasm, the more closely do inspiration and expiration approximate. The reverse is also true. After the physician has observed his

asthmatic patients closely, he will have some idea of the type of asthma he is dealing with.

In both spasm and dyspnœa, the personal factor is important, as some patients have the faculty, up to a certain point, of disregarding both. Dyspnœa is due to a combination of the blockage produced by the intrabronchial plugs and the action of the spasm and the cough, when present. Coughing accentuates the spasm. The dyspnœa of heavy breathing is much less than that of the actual attack. Pure spasm usually causes very little dyspnœa, unless deep-seated, when it can be a menace to life, especially when combined with the obstruction caused by heavy plugs. Pure spasm is often seen, when full expectoration is not followed by complete relief. It accompanies parsimony in the use of the sympathomimetic drugs.

In this stage, cough is a very important symptom and sign, but unfortunately is not always present. To read the text-books of years ago, one would imagine that cough was an essential feature of every attack. Many asthmatics now go through an attack without any sign of cough. When present, it is irritant and non-productive in type. In an attack, the cough is quenched by the sympathomimetic drugs. The clinical effect is to relieve the spasm, and leave the sputum where it is.

To complicate the picture, many patients carry, in addition, the signs and symptoms of general nasal infection. The groups of patients with this double picture are: (i) asthmatics with sinus disease, allergic or infective; (ii) asthmatics who have nasal polypi; (iii) asthmatics who have undergone major nasal surgery. Children with much nasal congestion of an allergic type accompanied by a coincidental infection form a special group never satisfactorily explained. Most are true asthmatics masquerading as bronchitics. In an occasional case the nervous symptoms are often predominant, while in the chronic variety wheezing and cough are the major symptoms, and spasm is a very minor one. Most are undiagnosed asthmatics. It is better to regard those asthmatics with nasal polypi as comprising a separate class of the disease, although the attacks follow the three-stage plan. Sinus infection is practically always present in these cases. Infection is not always seen in the sputum. I have had under observation an asthmatic with sinus disease who had a nightly attack of asthma for five years, without any so-called purulent sputum.

STAGE III.

When the spasm is completely gone, the patient enters the third stage. This part of the attack is generally forgotten and, indeed, there are many physicians who doubt its existence. Asthmatics, on the contrary, do not. Unless a sufficient amount of the sympathomimetic drug is given, the patient will be able to breathe, but the spasm will not be entirely gone. It is less intense, but still a powerful agent in preventing sleep. Half-treating the second stage only shortens the interval between attacks. The third stage commences with the disappearance of spasm, and finishes when the lung has been emptied as thoroughly as possible, and sleep begins. Sleep comes easily when the attack is over.

The sputum must be studied. It is impossible to take a patient through the third stage without this knowledge. Unless the second stage is completely relieved, the attack will not cease. A study of asthmatic sputum shows that the higher the sputum in the bronchial tree, the more watery and less viscid it is. As the centre of the allergic activity is deeper, it becomes more viscid and non-aerated. Finally, a stage is reached in which it is so viscid that the patient is unable to expel it. This is generally not seen in the earlier spasms of a sufferer, but in chronic cases after many months of frequent attacks, coupled with overuse of drugs and much misunderstanding about the disease. Those who have seen an autopsy on an asthmatic will recall the extreme difficulty of dislodging the sputum with the bronchi *in situ*.

There is a stage in which the sputum is not completely expectorated, and the patient has experienced a certain amount of relief. The patient is satisfied and the physician leaves, hoping that the relief will last, but fearing from past experiences that it may not. In this instance, there remain to be expelled the heavy airless plugs. These block the bronchi and keep an area of lung in a stage of partial or complete collapse. If these plugs are not expelled, the attack will soon return. These plugs are generally either mucopurulent in type or completely purulent, and sink like a stone in a basin of water. There is always a number of these for the patient to expectorate. Their size varies from that of a small pea to one larger than a walnut. They are expelled by the patient in an effortless sort of cough, very suggestive of the manner in which a patient with a tuberculous cavity expels its contents. The irritant cough does not seem to be as successful in dealing with these plugs as with the aerated mucoid and mucopurulent sputum, so often seen in the asthmatic with added chronic bronchitis.

MANAGEMENT.

Treatment is either physical, medicinal or dietetic.

Physical manœuvres are movements in which the patient may take an active or passive part. They are respiratory movements designed to relax the body muscles and to permit greater and more controlled movement of the diaphragm.

Massage of the chest muscles, combined with physical aid in breathing by manual help, is also used with success, especially in children. Breathing exercises and massage will help in the first stage only. They have their best use in the stage just before heavy breathing. Once retraction is seen in the suprasternal space it is too late, and not even worth a trial. These measures can, however, accentuate the spasm and tire the patient.

Medicinal Treatment.

Drugs used in treatment are classified according to the stage in which they are used. To confine the treatment of asthma only to Stage II is comparable to treating epilepsy only at the stage of convulsions. The well-known mixture of potassium iodide and stramonium is of great value in this regard. Its value is greatest when used between attacks and in the first stage.

In the second stage, the sympathomimetic drugs are supreme. No other group of drugs can bear comparison with them. Their double action in shrinking the mucous membrane and in releasing the spasm makes an airway and restores the inequality in respiration. These drugs, if used correctly and in sufficient dosage, will always put an end to Stage II. The physician must not forget that patients vary in their responses, some reacting more to the anti-spasmodic action and some more to the shrinking reaction. The individual reaction to adrenaline is a feature of this drug with asthmatics. The second point is, never send a boy on a man's errand.

There are cases in which the spasm is not very strong, and the dyspnœa is out of all proportion. Sometimes these cases are a disappointment with adrenaline, and the theophylline group of drugs produces a better reaction. To overcome this difficulty, many physicians use a combination of the two drugs. So great is the personal factor in asthma that the type of asthma and the reaction to the drug are peculiar to the individual.

Sometimes the physician will find that, although the spasm is not completely gone, the patient is not able to expectorate the sputum, and relief is not sufficient to allow him to enter Stage III. The indication is then for more aminophylline. Should wheezing persist, however, the indication is for more of the adrenaline type of drug.

Although there are many sympathomimetic drugs, adrenaline and ephedrine are outstanding. In most cases, it is not necessary to go outside them. Adrenaline is the best of this group. These drugs can be given singly or in combination. Generally, adrenaline is combined with ephedrine and ephedrine with isoprenaline.

Adrenaline.

Although the number of drugs of this nature is increasing, their efficiency has not to any great extent

increased. So much has been written about adrenaline that it would be advisable to review the methods of using this drug. First, never use any more or less than is necessary. Always begin with a small dose. In an adult, never begin with less than 0·3 ml. If there is no effect in 15 minutes, repeat the dose. Do not leave the needle in position, but choose a fresh area for every injection, at least an inch and a half from the previous one. Forget the adage of a minim per minute.

The physician can detect in the patient minor changes that will tell him whether and when the drug is having effect. First, there will be a blanching of the skin, not as marked as when the intravenous route is used, but still noticeable. In patients who have been using a lot of adrenaline, the facies is generally a muddy pale colour. Small amounts of adrenaline will have no effect on the facies or on the spasm in these patients. In most cases, there will be an increase in the pulse rate coupled with the advent of emotional and psychological signs such as lachrymation, vituperation and self-accusation. There will also be an accentuation, to a varying degree, of the asthmatic manifestations, particularly the intensity of the spasm and the range of respiratory movements. Should this effect be more than usually marked, the patient may be one in whom these symptoms overshadow the desired effect. This is the condition of adrenaline refractoriness, referred to later. If the practitioner will have the patience to watch for these signs and wait, he will find that respiratory relief follows soon after. After giving up to 0·60 ml. without relief, there is no point in waiting further unless the patient is a chronic asthmatic accustomed to adrenaline. Larger doses will have to be given, and the practitioner has to choose between a dose of, say, 1·50 ml., and the use of a method of enabling the drug to enter the circulation more easily. Small amounts of clear mucus may appear in the throat, but the greater amount of the sputum will remain in the bronchi.

In the belief that a small dose of adrenaline continually put into the circulation is better than large doses at long intervals, slow-acting forms of adrenaline have been made. These drugs are generally double strength, and should not be administered until the patient's tolerance is known. If this rule is not observed, much trouble in the shape of auricular fibrillation or collapse may follow.

If a physician meets a patient who administers his own adrenaline, trouble is ahead. If the drug is given by a relative, wife or husband, the usual position is that the patient has not had enough adrenaline. This is contrary to the situation in which the patient gives his own. Relatives will not take risks that the patient assumes with impunity. In all these cases, it is best to give a trial dose of adrenaline, preferably with hyalase, intramuscularly. Alternative to this is a mixture of 1 ml. of adrenaline (1 in 1000), ephedrine sulphate or hydrochloride (three-quarters of a grain) and hyalase (1 mg.) in a syringe, one-third of the total solution at a time being injected intramuscularly. The interval between injections should be about ten minutes, or the physician should wait until he is confident from his observations that relief is not coming. If this combination is not successful, the physician has two further means of approach. The first is to wait a little while in case there may yet be relief and, while waiting, use the methods outlined later to stimulate coughing, in the hope that the emptying of the bronchi will give a certain amount of relief, when the spasm will lessen. The second is to give a dose of adrenaline intravenously.

A common method of administering adrenaline is by means of a spray. This means that the patient can give himself large doses of adrenaline. The sprays are used in strengths up to 10% of adrenaline. There is no doubt as to the efficiency of this method; but unless the interval between the times of administration is quite a big one, there is always the danger that the patient will become adrenaline-resistant, and that the sputum will dry, so that the patient cannot possibly cough it up.

As there seems to be some doubt as to what is meant by adrenaline-resistant, I submit the following schema: (i) adrenaline-tolerant: the patient takes the injection of adrenaline without any untoward reaction; (ii) adrenaline-sensitive: the patient manifests an alarming response, mostly pulse irregularities, from tachycardia to auricular flutter, auricular fibrillation, and occasionally ventricular fibrillation with its inevitable result after the injection of less than the usual dose of 5 to 15 min.; (iii) adrenaline-resistant: in this condition the patient requires increasing quantities of the drug to achieve a satisfactory therapeutic response; (iv) adrenaline-fast: in this condition, the drug has no effect and the patient's condition is unchanged after an injection; (v) adrenaline-refractory: the beneficial effect is momentary, and just as the patient is beginning to improve, or even before that time, he is submerged in a flood of asthmatic symptoms even worse than the original condition for which he was treated. Patients in this condition are very close indeed to death. Faced with this situation, proceed as follows: do not give more adrenaline, but inject "Coramine" (one or two ampoules) intravenously; reassure the patient firmly and wait. On no account move the patient, or even alter his position in the slightest degree.

In children, adrenaline can be used as a liniment rubbed on the patient's chest. Adrenaline alkaloid or chloride is mixed in a vanishing cream to make a 1% mixture. This is gently rubbed into the skin of the thorax until absorption occurs.

Ephedrine.

This drug, in the form of the sulphate or the hydrochloride, is used by many physicians in preference to adrenaline. When used at the right time it will relieve most attacks of asthma. Failures are generally due to too small a dose. It will not relieve an intense and violent spasm in an asthmatic who has been administering his own adrenaline.

It can be given by mouth — the usual way — or given by intramuscular or intravenous injection. It is a constituent of practically every asthma remedy on the market. The dose usually prescribed is 0·5 grain, but this will relieve only the mildest of seizures. If it is given intramuscularly, it should be combined with 1 mg. of hyalase. If it is given intravenously, do not give less than three-quarters of a grain. Less than this is only wasting time, as the margin of safety is such that this amount can be given without fear. Ephedrine can be given intravenously straight from the ampoule. If it is given slowly, dilution is unnecessary. Its reaction time is longer than that of adrenaline, and it carries milder emotional effects. However, it is not entirely without these effects, as many patients have marked changes in temperament and approachability, not while the drug is exerting its major effect, but an hour or so later. They become difficult and belligerent, so that many of them have been termed contrary and unmanageable. Ephedrine has been combined with the isoprenaline group of drugs to prolong the effect. In other words, while the isoprenaline gives immediate relief, the ephedrine carries on.

Other Measures.

The isoprenaline group of drugs is extensively used by the medical profession, as they are quick-acting and have a simple method of administration. One of their main difficulties is that the mouth of an asthmatic in an attack is nearly always dry. The patient will find that if he keeps his mouth moist with sips of hot tea the effect is quicker and more effective. A tablet of 10 mg., crushed to powder, put under an upper denture and kept in position while the patient has a cup of hot tea and, if necessary, smokes a cigarette to stimulate salivation and expectoration, provides an efficient method of treating an unpleasant condition.

The therapeutic effect of the drugs just mentioned is aided by what are known as the prescription drugs, much less potent in controlling spasms. In addition, they loosen sputum and render the patient less liable to an attack. Every physician has his own special combination of drugs. The following is a prescription used by me for many

years: "Benadryl", 50 mg.; ephedrine hydrochloride, 0·75 grain; theobromin, 4·0 grains; caffeine alkaloid, 1·0 grain; potassium citrate, 10 grains; liquid extract of glycyrrhiza, 40 min. to half an ounce. Half an ounce is taken dissolved in three ounces of water. This is followed by a hot drink, of which the best type is easily tea.

Drugs are given by some physicians to loosen the sputum, although this practice is not as common as it was.

The popular mixture of potassium iodide and stramonium is of proven therapeutic value, enhanced by the addition of a small amount of ephedrine. This method of treatment is a little neglected, owing to the popularity of the new drugs. The action of these drugs is strengthened if steps are taken to empty the bronchi of sputum. All fluid should be consumed before 4 p.m., or at the very latest 5 p.m.; after that, its main effect will be to give the patient a restless night. If, in addition, ephedrine is taken, a bad night is a certainty.

The problem of loosening the sputum has been a foremost one for years. The discovery of wetting agents has helped. A useful member of this group is "Alevaire". The large inhaler is not practicable for most asthmatics, who must content themselves with small atomizers.

Hyalase can be added to the spray in the proportion of 2 mg. to 5 ml. of spray fluid. Penicillin can be added if there is proof of an infection of which the causative organism is penicillin-sensitive. Half a million units of penicillin may be added to about 5 ml. of the spray. For any benefit to follow the use of the spray, the patient must learn to use it correctly. It must be used only in inspiration. The patient must learn to time the spray with inspiration and to cease with expiration. For a patient struggling with his breath this is not easy and takes considerable practice. As "Alevaire" will not provoke a cough, it is possible to use the spray correctly and not get any sputum. Furthermore, the spraying must be nearly continuous throughout the spasm. As a spasm usually lasts an hour, an effort quite beyond the patient's capacity may be required. When in the second stage, if the patients find this to be the case, they do what asthmatics do with the greatest of ease — they give up and try something else easier and, they hope, better. Something more is necessary to provoke a cough and to make the sputum more fluid and less tenacious.

To aid the expulsion of mucus or sputum from the bronchi, there has been provided by Nature a powerful aid, to wit, the cough. Nothing should be done to allay or steady the cough.

The question of sedation and the use of the morphine, heroin, pethidine and similar drugs is one of perplexity. These drugs are generally used when the second stage gets out of hand, and the patient experiences the fear that the attending physician cannot control the attack. This happens when the physician is called late in the second stage to a patient who has been carrying out his own treatment. Mental distress seems to be the condition requiring assistance, and some practitioners use morphine and other drugs of this group to give the patient mental relief, and even relief from spasm. Many practitioners affirm that the spasm is relieved. By and large, these drugs are dangerous, and any practitioner who persists in using them will participate, sooner or later, in an unforeseen and unnecessary tragedy.

To produce or promote a cough means the inhalation of an agent with an inherent cough-producing quality. The well-known powders of lobelia and stramonium and the asthmatic cigarettes on the market are usually composed of these two constituents and potassium nitrate. As there are many asthmatics who already smoke, it is sometimes difficult to make them cough, and their asthma is, as a result, very difficult to relieve. The following is usually successful. A mixture of stramonium leaves, lobelia leaves and potassium nitrate in the proportion of 3 to 1 is made and placed on a piece of blotting paper. It is then rolled in the form of a cigarette and finally re-rolled in an ordinary cigarette paper. This cigarette will make any asthmatic cough, and will lead to no trouble.

Before using any agent to loosen the sputum, the physician must remember that the sputum is fixed when the spasm is on. In the first stage, the procedure is to administer the sympathomimetic drug, to wait 15 to 20 minutes, and then to use whatever method the physician prefers to loosen the sputum.

In the second stage, the physician must guard against using any means to loosen the sputum while the spasm's intensity is climbing. If he wishes to interfere at this stage, the dose of sympathomimetic drug must at least be doubled. If this is not done, the physician will find that the reactive effect of adrenaline and ephedrine will intensify the spasm.

When the spasm has reached its peak, or has begun to lessen, then it is safe to produce a cough and loosen the sputum. If, however, the physician decides to anticipate the peak, he asks for much trouble. One or two trials will soon teach him when to interfere in the attack.

Tobacco has been known for at least one hundred years as a powerful remedy in the treatment of asthma. The cough-provoking effect of tobacco on bronchi unsoiled by its smoke is very strong. In addition, and even more important, it stimulates a copious flow of watery and mucoid sputum. This is aerated, and its expulsion gives the patient relief. The inhalation of tobacco smoke at intervals will stimulate the cough, and greatly assist in emptying the bronchi. A trial will soon convince the practitioner of its efficiency in expelling the mucous plugs already described. Before an asthmatic smoker tries the cigarette recommended above, he should experiment with the various brands of cigarettes on the market, and he will soon find one to suit his requirements. To quote *The Lancet* (Volume 2, 1837):

> In disordered respiration due to asthma, tobacco obtained the well merited confidence of the older physicians in cases, where no organic alteration had occurred.

Tobacco has the great advantage of being available for treatment in the first stage, but not before the sympathomimetic drug has been taken. Once asthmatics have learned the stages, they will soon know when to start their treatment.

Most asthmatics who retire between the hours of 10 p.m. and midnight expect to be awakened by an attack at any time from 2 a.m. onwards. If they sleep the night through, they know that an attack will appear as soon as they awake, or very soon after.

There is a relation between the amount of sputum in the bronchi and the onset of the attack. It is very much easier to precipitate an attack in a bronchus full of sputum, than in an empty one. In asthmatics belonging to the 50 years and over age group, it is rare for a night to pass without an attack. The attacks vary, so that a night with a mild attack may be followed by a night with a severe one, and a late attack by an early one. Many asthmatics imagine that, because they have one or two nights with mild attacks, the disease is on the wane. Unfortunately, this is not so. As long as these asthmatics make certain of not allowing sputum to collect in the bronchi, the spasm will not advance in intensity, but will gradually diminish. In a little while they will be tempted to take risks.

Should any of the sympathomimetic drugs be taken, the instructions already given should be followed. Let the asthmatic have no false ideas. As long as he is in the category mentioned above, there is always sputum in his bronchi, whether an attack is on or not. It is well for this type of patient to learn the lesson early and bring on his attack early several hours before it is due, and convert it into asthma *de convenance*. He will be surprised by the amount of sputum that he has to expectorate. As was mentioned above, it takes three days to empty the bronchi after a single attack. When the bronchi are empty, the trigger is much more difficult to pull.

Sometimes sleep is slow in coming, and the patient may become restless. He is even restless when asleep. It generally happens this way when the patient has allowed

the attack to go too far before attempting any treatment, or has not used enough adrenaline or ephedrine. However, if he sleeps till the morning, he will find the attack completely gone, and the day will be clear of further attacks. Sleep does not cure any form of allergy.

Relaxation of spasm alone will not give complete relief.

Complete relief is something that many asthmatics have not experienced for years. I am now referring mainly to the asthmatics aged over 50 years.

If the sputum is not removed, the spasm will return when the action period of the drug disappears. Removal of the sputum alone will not give complete relief, but at least it will last for a longer period. Combination of the two is best.

Conclusion.

In general, the main steps in treatment are: (i) complete relaxation; (ii) relief of the spasm with appropriate drugs; (iii) stimulation of the cough; (iv) promotion of expectoration.

The routine of bringing on an attack in the first stage must be carried out every night; but the patient will find that, as he persists, the amount of sputum gradually becomes less, and the sputum is also less viscid and easier to expel. Plugs will be fewer and fewer and their character changes.

For patients who are regularly taking cortisone, this method has a special appeal. It is better to have a mild occasional attack and empty the bronchi, than to take large doses of cortisone and suppress every attack. Should the patient use this method, he will find that the attack is milder, and in addition, his daily requirements of cortisone are less. Asthmatics know that when they stop having A.C.T.H. or cortisone, the attacks may recur with increased strength. The practice of inducing mild attacks renders this possibility less likely. Furthermore, when a patient begins treatment with A.C.T.H. or cortisone, it is wise to empty the bronchi in the early stages.

A final word to all practitioners: a patient in the middle of an asthmatic seizure feels very ill. If the attack has lasted several hours and much adrenaline and similar drugs have been given, he can be, and often is, dangerously ill. His frame of mind is one of hopelessness and dejection. He is tired of these attacks with their severity and regularity. Be very guarded with your remarks after you have given adrenaline or ephedrine. The patient's mental processes and reasoning powers are not crystal-clear, and he can be easily made non-cooperative and hostile. Listen to what he says, help him, and leave all discussion till next day.

SERUM URIC ACID.[1]

By Peter I. A. Hendry, D.C.P. (Lond.), M.C.P.A.,
Kevin H. White, D.C.P. (Lond.), M.C.P.A.,
and
Ian J. Stanger, A.A.I.M.L.T.,
Newcastle.

The number and variety of methods recommended for the estimation of uric acid in blood suggests that no one method is entirely satisfactory.

Caraway (1955) published a method which appealed because it dispensed with cyanide, it was simple, and strict control of working conditions was unnecessary. The object of this investigation was to evaluate its use as a routine laboratory procedure and to establish a normal range.

Method.

The method is briefly as follows. The serum proteins are precipitated by a solution containing a mixture of sodium tungstate and sulphuric acid. A sodium carbonate solution is then added to the centrifugate or filtrate and to a blank. Dilute phosphotungstic acid is added and the mixture allowed to stand for 30 minutes. The unknown is

Table I.

Uric Acid Concentrations (Mg. per 100 ml.).

Uric Acid Concentrations.	Standard A Dilution.	Standard B Dilution.
2	4	4
4	2	2
5	2	2
6	2	2
7	2	2
8	2	2
10	4	4
12	4	4
14	2	2
15	2	2
16	2	2
17	2	2
20	2	2

then read against the blank with the use of a red filter. The concentration of uric acid is read from a calibration curve.

Success of the method, according to Caraway, depends on the use of a much-diluted solution of phosphotungstic

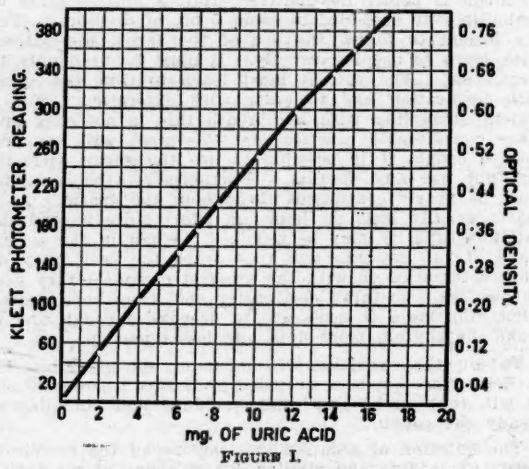

Figure I.

Uric acid calibration curve.

acid, with the addition of sufficient sodium carbonate to buffer the final mixture at a pH approximating the pK_2 of carbonic acid.

Class B glassware was used throughout. A Klett-Summerson photoelectric colorimeter, which has a log-

Table II.

Serum Uric Acid Concentration in Pooled Sera.

Pool.	Number of Tests.	Range. (Mg./100 ml.)	Mean. (Mg./100 ml.)
A	6	5·3 to 5·7	5·6
B	5	5·3 to 5·4	5·4
C	12	5·0 to 5·4	5·2
D	3	5·6 to 5·6	5·6
E	10	5·1 to 5·6	5·4

arithmic scale proportional to the optical density, was used. The red filter used was the Klett-Summerson red filter number 66 (range 640 to 700 mμ.).

Precipitating Reagent.

Caraway uses a precipitating reagent consisting of 700 ml. of water, 100 ml. of a 10% solution of sodium tungstate

[1] Read at the annual meeting of the College of Pathologists in August, 1958.

and 100 ml. of two-thirds normal sulphuric acid, to which he adds as a stabilizer 0·05 ml. of an 85% solution of phosporic acid— 9·0 ml. of this is added to 1·0 ml. of serum. This reagent develops a colour on standing which, however, is removed during the precipitation of the proteins. When fresh, the reagent has a constant optical density of 0·01, and is used as the blank. When the optical density rises, the reagent is discarded and a fresh solution prepared. Colour development in this reagent is diminished if kept in the dark. This reagent was used throughout the investigation.

When whole blood and serum were compared, it was found that Caraway's precipitating reagent was of no use;

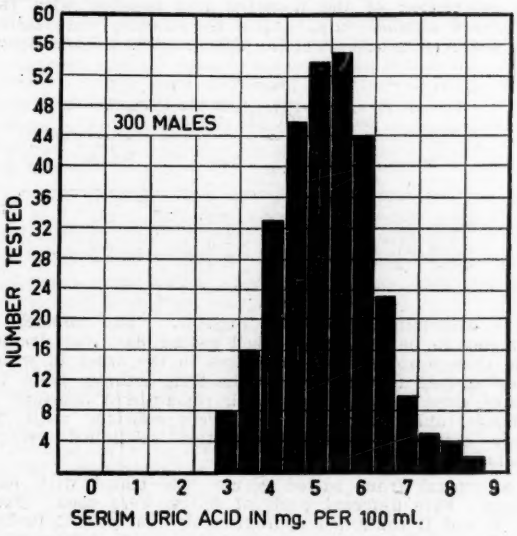

FIGURE II.
Uric acid concentrations in serum from 300 males.

results on whole blood were higher than results on serum from the same person. However, we did find that a precipitating reagent for unlaked blood described by Folin (1930) gave consistent results when whole blood was compared with serum; serum always gave a higher result than whole blood, the difference being apparently related to the hæmatocrit.

The two precipitating reagents were then compared on numerous samples of serum and the results using each reagent were identical.

The Folin's precipitating reagent for unlaked blood consists of eight volumes of sodium sulphate-sodium tungstate mixture, one volume of test solution (whole blood, serum, etc.), and after mixing and standing five minutes the addition of one volume of one-third normal sulphuric acid. The sodium sulphate-sodium tungstate mixture consists of 15 grammes of anhydrous sodium sulphate plus six grammes of sodium tungstate ($Na_2Wo_4.2H_2O$) to the litre.

Working Standards.

It was found that aqeuous standard solutions of uric acid were not always satisfactory, as even in concentrated solution with chloroform added they occasionally deteriorated, though kept in the refrigerator. On the other hand, pooled serum kept well in the refrigerator and gave consistent results, even after storage, for periods up to three months. Throughout the investigation, pooled serum was used as a control, together with a working standard.

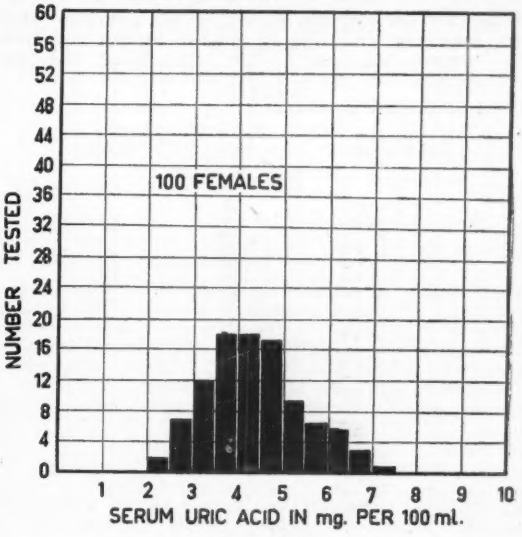

FIGURE III.
Uric acid concentrations in serum from 100 females.

Calibration Curve.

As no A.R. quality was available, four batches of uric acid from different manufacturers were compared. From each batch standards were prepared equivalent to 5 mg. of uric acid per 100 ml. Each standard was tested in duplicate, and the photometer readings were compared. The results were as follows: batch A, 119 and 120; batch B, 121 and 123; batch C, 119 and 121; batch D, 120 and 121. It was concluded that there was no significant difference between batches.

One batch was then selected and from it two stock standards were prepared. For one standard (A), 0·1 mg. of uric acid was dissolved in 500 ml. of diluent; for the other (B), 0·2 mg. of uric acid was dissolved in 1000 ml. of diluent. From each standard dilutions were prepared equivalent to several concentrations of uric acid. The

TABLE III.
Results of the Survey.

Age Group. (Years.)	Males.			Females.			Total.		
	Number Tested.	Range.	Mean.	Number Tested.	Range.	Mean.	Number Tested.	Range.	Mean.
20 and under ..	17	3·3 to 6·6	5·0	16	2·7 to 6·6	3·7	33	2·7 to 6·6	4·4
21 to 30 ..	60	3·1 to 8·9	5·6	21	2·8 to 6·3	4·1	81	2·8 to 8·9	5·2
31 to 40 ..	96	3·2 to 8·5	5·5	19	2·2 to 6·2	4·1	115	2·2 to 8·5	5·2
41 to 50 ..	85	3·2 to 8·7	5·3	26	2·9 to 7·4	4·6	111	2·9 to 8·7	5·1
51 to 60 ..	33	3·2 to 8·0	5·5	16	2·6 to 6·5	4·4	49	2·6 to 8·0	5·1
Over 60 ..	9	3·8 to 7·5	5·9	2	4·7 to 6·2	5·4	11	3·8 to 7·5	5·8
Total ..	300	3·1 to 8·9	5·4	100	2·2 to 7·4	4·25	400	2·2 to 8·9	5·15

number of these dilutions from each standard and for each concentration are set out in Table I. The uric acid concentrations refer to the equivalent concentrations of uric acid in a blood sample tested.

The optical densities of the dilutions at each concentration were averaged and the figures obtained were plotted on ordinary graph paper against the uric acid concentration (Figure I). At any particular uric acid concentration the photometer readings of all dilutions at that concentration varied from a minimum of ±0·2% to a maximum of ±3%. The calibration curve was practically a straight line to a concentration of 10 mg. per 100 ml

Serum or Whole Blood.

Feichtmeir and Wrenn (1955), using a uricase technique, found no uric acid in washed human red blood cells. The true uric acid level in whole blood, then, will vary with the hæmatocrit. In this survey Folin's precipitating reagent for unlaked blood was used and no uric acid was detected with washed red cells.

TABLE IV.

Uric Acid. (Mg./100 ml.)	Number of Males.	Number of Females.
2·1 to 2·5	—	2
2·6 to 3·0	—	7
3·1 to 3·5	8	12
3·6 to 4·0	16	18
4·1 to 4·5	33	18
4·6 to 5·0	46	17
5·1 to 5·5	54	9
5·6 to 6·0	55	7
6·1 to 6·5	44	6
6·6 to 7·0	28	3
7·1 to 7·5	10	1
7·6 to 8·0	5	—
8·1 to 8·5	4	—
8·6 to 9·0	2	—
Total	300	100

Bensley, Mitchell and Wood (1947), using an electrophotometric modification of Folin's direct manometric method, found that the recoveries of uric acid from serum were higher and less variable than those from whole blood. The whole blood values were equal to or higher than serum values in 15 of 100 normal specimens tested. In the remaining 85 normal specimens, the whole blood figures were lower than those for serum.

Jacobson (1938) showed that unlaked blood filtrates were unsatisfactory, because they yielded values which were influenced by a variable degree of extraction of chromogenic material from the red cells.

Natelson and Kaser (1953), supporting the use of serum rather than of whole blood, pointed out that there is a substance in red cells which may inhibit the development of colour and that reducing substances are present in relatively high values in red cells.

From this evidence it is obviously more accurate and safer to use serum rather than whole blood. Further, serum should be separated from the blood clot, and hæmolysis must be avoided.

The Survey of Normal Specimens.

The survey of normal specimens was performed on serum obtained from blood donors of the Royal Newcastle Hospital Blood Bank; 300 males aged between 16 and 65 years and 100 females between 18 and 69 years were tested. Each sample was collected from the donor at the completion of the donation and labelled with the registered number only. After the samples were tested and the results tabulated, the age and sex of each donor were ascertained from the register. The number of samples to be collected each bleeding day was decided and they were taken from donors in the order in which they arrived to donate. By the time samples from 300 males were collected there still remained a shortage of females, and then these only were collected until 100 were obtained. The investigation continued over a period of six months.

TABLE V.

Normal Range of Uric Acid Concentration in Serum (Mg. per 100 ml.).

Normal Range.	Male.	Female.
Lower 1%	3·2	2·2
Lower 10%	4·1	3·1
Upper 10%	7·0	6·0
Upper 1%	8·5	6·8

A control from pooled serum was tested with each batch. Five different pools of serum were used. Pools A, B and D contained approximately ten, pool C twenty, and pool E thirty lots of serum also obtained from blood donors. Thirty-six tests were performed with the use of the five pools of serum, and the results were consistent, as indicated in Table II.

Results.

The results of the survey are summarized in Figures II and III and in Table III. The histograms were constructed from the results as shown in Table IV.

The difficulty of establishing a normal range is appreciated. Using 400 blood donors, it is possible that some may have abnormal uric acid concentrations. However, it is difficult to decide which should be eliminated. It is thought that the method suggested by Wootton and King (1953) has advantages. They suggest stating the

TABLE VI.

Quoted Normal Uric Acid Levels in Plasma and Serum (Mg./100 ml.).

Sample.	Number Tested.	Sex.	Author.	Method.	Range.	Mean.
Plasma.	?	M.+F.	Jacobson (1938).	Folin.	2·0 to 6·9	4·2
Plasma.	?	F.	Bulger and Johns (1941).	Uricase.	2·0 to 6·0	3·5
Plasma.	?	M.	Bulger and Johns (1941).	Uricase.	2·0 to 6·0	4·4
Plasma.	33	M.	Brehner-Mortenson (1940).	Flotow.	4·6 to 8·8	—
Plasma.	21	F.	Johnstone (1952).	Uricase.	2·0 to 6·5	3·7
Plasma.	17	M.	Johnstone (1952).	Uricase.	2·8 to 7·0	4·6
Serum.	?	M.+F.	Leone and Manzi (1947).	Uricase.	5·0 to 6·0	—
Serum.	51	M.+F.	Natelson and Kaser (1953).	Brown.	2·4 to 5·9	4·3
Serum.	52	M.+F.	Caraway (1955).	Caraway.	3·0 to 5·5	—
Serum.	44	F.	Feichtmeir and Wrenn (1955).	Uricase.	—	3·75 (S.D.=1·11)
Serum.	35	M.	Feichtmeir and Wrenn (1955).	Uricase.	—	5·89 (S.D.=0·86)
Serum.	48	F.	Alper and Seitchik (1957).	Archibald.	2·6 to 5·4	4·0
Serum.	95	M.	Alper and Seitchik (1957).	Archibald.	3·8 to 7·1	5·4
Serum.	100	F.	This survey (1958).	Caraway.	2·2 to 6·8[1]	4·3
Serum.	300	M.	This survey (1958).	Caraway.	3·2 to 8·5[1]	5·4

[1] Of the females, 98% fell between 2·2 and 6·8 mg. per 100 ml., and of the males, 98% fell between 3·2 and 8·5 mg. per 100 ml.

normal range as follows: lower 1%, lower 10%, upper 10%, upper 1%.

In this survey the figures would be as shown in Table V.

Wootton and King suggest that in clinical practice any result falling outside the 10% limits is considered suspicious; a result which falls outside the 1% limit is almost certainly abnormal.

The results obtained are compared with findings obtained by different authors using a variety of methods (Table VI).

Conclusions.

It is generally considered that only uricase methods give "true" uric acid values and that other methods give higher figures.

Alper and Seitchik (1957) found little significant difference between the results obtained by the method they recommend and the uricase method, with which they compared it. Also, their results were almost identical with those found in this survey.

Feichtmeir and Wrenn (1955), using a uricase method, obtained figures slightly higher than those obtained in this survey.

Uricase methods, then, do not apparently give "truer" uric acid values, and they require the use of ultra-violet spectrophotometers. Caraway's method is extremely simple and reliable, and eliminates the use of cyanide.

Caraway's method is therefore strongly recommended for routine laboratory use.

Summary.

Caraway's method of uric acid determination, using sodium carbonate instead of cyanide, has been investigated and, as the author claims, it is simple and reliable. It yielded consistent reproducible results with the use of a calibration curve. A control serum as well as the working standard is advised.

The uric acid concentration in the serum of 300 apparently normal males and 100 apparently normal females was investigated. The results were tabulated and histograms constructed.

The serum uric acid concentrations of 80% of the male blood donors lay between 4·1 and 7·0 mg. per 100 ml. and 98% between 3·2 and 8·5 mg. per 100 ml. Of the female donors, 80% lay between 3·1 and 6·0 mg. per 100 ml. and 98% between 2·2 and 6·8 mg. per 100 ml.

The normal range is discussed. Females showed consistently lower figures than males. Age, with the possible exception of the under twenty age group, did not appear to influence the serum uric acid levels. These figures were not submitted to statistical analysis.

Acknowledgement.

We wish to acknowledge the assistance of those who, by their criticisms, helped to shape this paper. The drawings of the calibration curve and the histograms were prepared in the clinical photographic unit of the Royal Newcastle Hospital.

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Reports of Cases.

ACUTE BILATERAL FOOT-DROP IN CHILDREN.

By J. W. LANCE,

From the Neurology Clinic, Sydney Hospital, Sydney.

THE purpose of this communication is to describe the clinical histories of two children who present a similar and distinctive clinical problem.

Acute bilateral foot-drop in children is commonly part of a pattern of extensive muscular weakness, as in acute anterior poliomyelitis or in the Guillain-Barré syndrome, so that its occurrence as an isolated phenomenon is of considerable interest. The condition is apparently unusual in neurological practice, judging from the experience of colleagues and the paucity of information in the literature.

Case 1.

A girl, aged 11 years, was normally healthy, a good athlete and swimmer. The day before her school sports day, early in August, 1958, she developed aches in both calves. The next day she competed in spite of this, but did not perform well. She was accustomed to clear 4 ft. 3 in. in the high jump, but on this occasion was disqualified on the first jump with the bar at 3 ft. 6 in. She came about sixth in the 75 yards race, instead of second or third as she would normally have anticipated. The next day, her calves felt very sore and stiff. This feeling persisted for about a week, when she noticed that her feet seemed "floppy", and her parents saw that her gait was peculiar, her feet being lifted higher than usual. Her calf soreness resolved at the onset of foot-drop.

Questioning of the patient disclosed that she had not experienced headache, backache, paræsthesiæ, girdle sensations or other symptoms. Her past health had been free of serious illness. Three months before the onset of her first symptoms she had been involved in an accident, when the bicycle which she was riding was hit by a motor-car. She was not knocked unconscious, although she was temporarily "dazed and hysterical"; she suffered abrasions to the left side of the face and to the legs, which were treated with a mercurial ointment. Six weeks after this, she developed pain in the left shoulder, which took a fortnight to clear up. She had completed her course of immunization against acute anterior poliomyelitis, the last injection having been given seven months before the illness, and had not received any other injections in the preceding year. Her menstrual periods had started five months before the present illness. Her mother and father were in good health, and there were two brothers and one sister, all of whom were well.

Physical examination was carried out three weeks after the onset of weakness. The patient was a bright, attractive girl, well developed for her age, who walked with a high-stepping gait. She was unable to balance when her feet were together, whether her eyes were open or closed. Her fundi oculorum, cranial nerves and upper limbs were normal. Examination of her lower limbs showed flaccid

paralysis of ankle dorsiflexors and evertors, with some weakness of plantar flexion and toe flexion, which was later charted by the physiotherapy department of Sydney Hospital (in accordance with the Medical Research Council Scale, ranging from 0 to 5) as follows:

	Right	*Left*
Tibialis anterior	0	0
Extensor hallucis longus	0	0
Extensor hallucis brevis	?1	0
Extensor digitorum longus	0	0
Extensor digitorum brevis	0	0
Peroneus longus	4	1
Triceps suræ (gastrocnemius and soleus)	4+	4
Tibialis posterior	4	4
Flexor digitorum longus	2	0
Flexor hallucis longus	0	0

Her deep tendon reflexes were all present and equal, the ankle jerks being a little less brisk than the others; the plantar responses were flexor. There was no loss of sensation to touch, pin-prick or vibration; joint position sense was unimpaired.

General examination revealed no abnormality.

The patient was admitted to Sydney Hospital, where the following tests were performed. Lumbar puncture was carried out, and clear fluid was obtained at 120 mm. pressure. There was no increase in cells, the protein content was 30 mg. per 100 ml. and the Wassermann reaction was negative. When a blood count was made, the hæmoglobin content was found to be 15·0 grammes per 100 ml. A blood smear was normal and no stipple cells were seen. X-ray examination of the chest revealed no abnormality. The urine did not contain porphobilinogen. Lead excretion on two occasions was within normal limits (0·02 mg. and 0·04 mg. per 24 hours).

The patient was considered to have motor neuritis of unknown cause, and was given a course of prednisone tablets, 10 mg. twice daily, tapering off after one month. She was fitted with calipers and toe-raising springs and given plaster "boots" to be applied at night, and continued physiotherapy on returning home.

No change occurred until five months had elapsed, when she noticed that she could wriggle her right great toe. One month later she could move all the toes of the right foot and the great toe of the left foot. Improvement continued steadily, sufficient for her to play hockey again eight months after the start of her illness. However, a review examination nine months from the onset showed that there was still considerable weakness of dorsiflexion of the left foot, which could be elevated only a few degrees against gravity, although it moved almost to right angles when she was lying flat. Eversion of the foot and toe-flexion were weak, although plantar flexion of the foot was normal. The right lower limb had almost fully recovered. The left ankle jerk was less brisk than the right, and sensation remained normal.

Electromyography was carried out at this juncture, and normal responses were obtained from the right anterior tibial group. On the left side, fibrillation potentials were recorded at rest, the interference pattern was abnormal and motor unit potentials showed considerable polyphasic activity, with a proportion of giant potentials; these findings indicate the presence of a lower motor neurone-lesion. The patient would not tolerate nerve stimulation, so that estimation of conduction time was not possible.

Case II.

A boy aged eight years, was healthy and active until, in mid-November, 1958, he became aware of soreness in both calves, which continued for a week; at that stage his parents noticed that he was dragging his feet. This was first attributed to a new pair of sandals with rubber thongs which he had recently been wearing, so that no action was taken by his parents for some weeks. He was examined three weeks after the onset of bilateral foot-drop, and questioning disclosed that he had not suffered paræsthesiæ, sphincter disturbance or other relevant symptoms. Two weeks after the onset he had developed a cold and sore throat, but no signs of infection had been noticed before weakness became apparent. A measles epidemic was in progress in the neighbourhood, but there was no story of direct contact. He had been given his third injection of Salk vaccine six months before the start of his illness. Inquiry into his past health and family history contained nothing of note.

On examination, he was found to have no power of dorsiflexion or eversion of either foot, and the extensor hallucis longus was functionless on both sides; slight extension of the other toes was possible. Flexion of the toes and plantar flexion appeared normal. There was no loss of sensibility for touch, pin prick, joint position or vibration. The deep tendon reflexes were active and symmetrical, including the ankle jerks; the plantar responses were flexor. The remainder of the nervous and other systems were normal on full examination.

A number of investigations were carried out. A full blood count gave normal results, the hæmoglobin value being 13·0 grammes per 100 ml. The patient's erythrocyte sedimentation rate, determined by the Westergren method, was 7 mms. in one hour. His urine was found to be free from porphyrins, and the centrifuged deposit appeared normal. A 24 hour specimen contained 0·03 mg. of lead per litre, a figure within normal limits. Lumbar puncture was not considered necessary at the time. Electromyography was carried out, and needle electrodes inserted in the right anterior tibial group of muscles recorded marked fibrillation potentials; on attempted movement, there were occasional abnormal muscle potentials. Electrical stimulation of the peripheral nerves was attempted, but no estimate of nerve conduction time could be made, as the patient found it hard to cooperate. A specimen of stool collected some four weeks after the onset of symptoms was examined by tissue culture (human amnion and HeLa cell) which did not demonstrate virus growth. Samples of serum were taken four weeks and six weeks after the onset of foot-drop, and complement-fixation tests for the three main strains of poliomyelitis virus were carried out. The titres were identical in both samples, being less than 1:20 for Type I, 1:20 for Type II and 1:80 for Type III. These titres are sufficiently low to make it highly unlikely that the illness was caused by a poliomyelitis virus.

The patient was fitted with calipers, toe-raising springs and plaster boots for night wear. Four and a half months after the onset of the illness he had improved sufficiently to dorsiflex both feet against gravity, but they could resist only slight pressure. At seven months some weakness of dorsiflexion and eversion of the feet and extension of the toes was still present (4·5 on the MRC scale). The mid-calf circumference had diminished from 10·5 in. at the initial examination to 9·75 in. on both sides.

Discussion.

These two children presented themselves with a history of calf soreness of one week's duration, followed by the sudden onset of bilateral foot-drop, which has gradually decreased over the respective periods of eight months and eleven months for which they have been observed. There was no sensory disturbance, and reflexes were preserved. Electromyography confirmed the clinical diagnosis of a lower motor neurone disturbance in each case, thus eliminating hysteria, myositis and myopathy, which were other possibilities considered.

The distribution of the lesion implicated the anterior horn cells and motor nerve roots of the fourth and fifth lumbar and first and second sacral cord segments, or the popliteal branches of the sciatic nerve, or both sites. In Case I, the weakness was more extensive than in Case II, and included the plantar and toe flexors.

The ætiology of this condition may be considered under the following headings.

Acute Anterior Poliomyelitis.

There was no prodromal systemic disturbance in these patients, or any indication of meningeal irritation. The

paralysis was symmetrical and limited. Both children had received their final injections of Salk vaccine some six months before the onset of the disorder; it is thus possible that the illness was a mild attack of poliomyelitis, rendered atypical by partial immunity. The results of complement-fixation tests for the three main strains of poliomyelitis virus on the second patient's serum do not support this, but unfortunately the patient was not seen until three weeks after paralysis appeared, so that no adequate control sample of serum could be obtained.

Radiculitis.

Paralytic brachial radiculitis (neuralgic amyotrophy) is a quite common condition causing pain over the shoulder and arm, followed by weakness and wasting of segmental or peripheral nerve distribution in the affected limb. There may be sensory loss over the area supplied by the circumflex nerve, or patchy dermatomal changes.

Lumbo-sacral radiculitis is much less common, and is usually accompanied by sensory loss and sphincter disturbance (Cramer, 1934; Ironside, 1951). Elsberg and Constable (1930) investigated 45 patients with cauda equina lesions; laminectomy revealed that 28 of these had tumours compressing the nerve roots, and the other 17 showed signs of inflammation. Foot-drop was noted in three of the latter patients. None of the group with radiculitis was under the age of 20 years, and in most cases the condition had a slowly progressive onset, and caused sensory loss and alteration of sphincter control.

Parsonage and Turner (1948) described 136 patients with the clinical picture of neuralgic amyotrophy affecting the shoulder girdles. They state that "it is doubtful if any comparable condition occurs in the lower limb; isolated external popliteal-nerve lesions are common, but many of these are pressure palsies, and in the cases where there is no evidence of pressure there has rarely been any pain". Garland (1957) has recently described a motor disturbance of the lower limbs which resembles neuralgic amyotrophy of the upper limbs. However, this condition affects proximal muscles more severely, and as it occurs in association with diabetes, it has been termed "diabetic amyotrophy".

Acute "Infective" Polyneuritis (Guillain-Barré Syndrome).

The Guillain-Barré syndrome usually follows a febrile episode, and motor involvement is more conspicuous than sensory.

Gilpin, Moersch and Kernohan (1936) reported 35 cases, and tabulated details of 20 of these with cerebro-spinal fluid findings. They commented that muscular weakness was invariably more marked in the distal parts of the limbs. In two of their cases weakness was limited to the lower limbs. One of these patients was an adult who also had sensory loss, but the other was a girl, aged 12 years, who complained of pain in the legs one week after a feverish illness, and whose legs were "slightly affected" without sensory loss. Reflexes were diminished and the level of protein in the cerebro-spinal fluid was 120 mg. per 100 ml.

Casamajor and Alpert (1941) have reviewed the problem of the Guillain-Barré syndrome in children, and summarized the 19 cases reported in the English literature, adding three cases of their own. They consider that weakness is more profound in the proximal portion of the limbs, as distinct from the views previously discussed. They quote the case described above, and that of another child, aged three years, reported by Bassoe (1938), with "atrophy of leg muscles below the knees"; however, Bassoe's description of the illness suggests arachnoiditis of the posterior fossa and upper cervical part of the cord, rather than the Guillain-Barré syndrome. Weakness was at first limited to bilateral foot-drop, but progressed until the left arm and left leg could not be moved. A cisternal myelogram showed an upper cervical block, and the cerebro-spinal fluid protein level ranged from 2000 to 6600 mg. per 100 ml. Papilloedema was present, and ankle clonus appeared later, when the plantar responses became extensor. Considerable recovery eventually occurred.

Apart from the case reported by Gilpin, Moersch and Kernohan mentioned above, I have been unable to find any case recorded in the literature which resembles those described in this paper. The usual features of the Guillain-Barré syndrome have recently been reviewed in this Journal by Wolfenden and McGuinness (1958).

Acute Polyneuritis from other Causes.

Polyneuritis may occur with many of the specific infectious fevers of childhood, and in intoxication by metals, organic chemicals or drugs. There was no history of a recent exposure to infection or toxin in the cases presented here. Lead poisoning was specifically excluded by investigations, as it may produce a localized motor deficit without sensory change, although the disturbance is usually more generalized in childhood (Ford, 1952).

Serum sickness may be associated with motor neuritis (Allen, 1931); but there was no evidence of allergic disorder in these children, and they had not received any injections since their Salk vaccine.

Motor neuritis, usually widespread, is seen in porphyria. There was no history of abdominal pain in these cases, and the urine contained no porphobilinogen. There was no suggestion of vitamin deficiency or other metabolic disorder.

Peroneal muscular atrophy and other familial neuritic diseases may present as bilateral foot-drop, which runs a chronic and slowly progressive course. Compression of the lateral popliteal nerve is not uncommon as a cause of unilateral foot-drop, and is usually responsible for limited sensory loss as well; compression neuritis of the sciatic or popliteal nerves would have to be bilateral to explain the deficit in these cases, and can reasonably be excluded on the history alone.

Considering all these possibilities, the most probable diagnosis appears to be motor neuritis of allergic or viral ætiology. As these patients presented within three months of one another, it is likely that there have been a number of such cases in the community. Correlation of information about any similar cases observed by other practitioners will help to clarify the clinical picture. Prompt virus studies on stools and serum of future patients may determine whether this is a variant of some recognized disease, or a newly-arisen syndrome eligible to adopt one of the increasing band of orphan viruses.

Summary.

The clinical histories of two children with acute symmetrical bilateral foot-drop are described.

The onset of foot-drop was preceded by soreness in the calves for one week, and was notable for the absence of sensory loss and the preservation of reflexes.

Both children had completed their course of Salk vaccine some six months before their illness started. Considerable recovery has taken place during the respective periods of eight months and eleven months for which these patients have been observed.

The condition appears to be a type of motor neuritis, and the ætiology is discussed.

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ACUTE SALT DEPLETION IN FIBROCYSTIC DISEASE OF THE PANCREAS.

By WILLIAM A. C. DOUGLAS,
Brisbane Children's Hospital, Queensland.

THE purpose of this paper is to draw attention to the severe upset in electrolyte balance which may occur in infants and children who are afflicted with fibrocystic disease of the pancreas. Kessler and Andersen (1951) were the first to describe acute vascular collapse in a number of these patients during heat-wave conditions, but they were unable to offer a satisfactory explanation for the disturbance of physiology involved. Di Sant'Agnese, Darling, Perera and Shea (1953) demonstrated excessive loss of sodium and chloride in the sweat of children with fibrocystic disease. These authors found that the concentration of salt in the sweat of these patients could be as much as four times that of the normal child, and that excess loss could lead to acute salt depletion in hot weather. Work by Darling, Di Sant'Agnese, Perera and Andersen (1953), and by Shwachman and Gahn (1956), has confirmed these findings.

The climate of large areas of tropical and sub-tropical Australia provides, during the summer months, the requisite conditions for this complication to occur in children suffering from fibrocystic disease of the pancreas, but no reports of acute salt depletion as a complication of this disease have appeared in Australian literature. Two cases which have occurred in Queensland within a short period recently are therefore reported.

Clinical Records.

CASE I.—The patient was a female, aged four years. A diagnosis of fibrocystic disease of the pancreas had been made twelve months previously based on failure to thrive, chronic chest infection, steatorrhœa, absence of trypsin from the duodenal juice and a sweat chloride value of 130 mEq/l. (normal range 4 to 80 mEq/l.). There was no family history of this disease.

The child presented at the Brisbane Children's Hospital at 2 a.m. on November 1, 1958. Maximum climatic temperatures of 105° F. and 98° F. had been recorded in Brisbane on the two previous days (October 30 and 31). The child had appeared to be well until 5 p.m. on October 31, when she vomited several times.

On arrival at hospital, the patient was afebrile, conscious, apprehensive and in severe peripheral circulatory failure. Her eyes were sunken, the extremities were cold and the radial pulse was impalpable. She was noted to have pink lips and a moist tongue, and to be sweating excessively. No focus of infection was detected.

Fluid was given intravenously in the form of 50 c.cm. of a 25% solution of albumin and 500 c.cm. of half-strength physiological saline immediately followed by a maintenance dose of one-fifth strength physiological saline with 5% glucose. This resulted in a dramatic improvement in her clinical state.

The serum electrolyte levels six hours after intravenous therapy was commenced were: sodium, 129 mEq/l.; chloride, 75 mEq/l.; potassium, 4·5 mEq/l. Intravenous therapy was ceased on November 2, and estimations of the serum electrolyte levels repeated two days later were normal (sodium, 143 mEq/l.; chloride, 101 mEq/l.; potassium, 4·5 mEq/l.).

The child was discharged from hospital on a maintenance oral dose of four grammes of salt daily in addition to her normal intake.

CASE II.—The patient was a female, aged ten months. She was referred from a north-western Queensland town, and was admitted to this hospital on November 13, 1958.

The family history yielded the following information. The patient was the youngest of ten children. One male sibling died at the age of fourteen months from clinically proven fibrocystic disease of the pancreas. A second male sibling died, aged eighteen months, and was suspected of having fibrocystic disease.

The patient had a past history of persistent cough and wheeze and several mild attacks of bronchitis. Her weight gain was satisfactory, and the stools were macroscopically normal.

Maximum daily climatic temperatures recorded in the town from November 3 to November 7 ranged from 101° F. to 107° F.

The child had appeared well until November 5, when her mother noticed that she was listless and had sunken eyes. On November 7 she vomited several times, and was seen by a local medical practitioner who described her as "moribund, severely dehydrated and in a cold lather of perspiration". The patient's temperature then was 103° F. A provisional diagnosis of septicæmia was made, and intravenous fluids and antibiotics were administered. The child failed to respond adequately, and was transferred to the Brisbane Children's Hospital.

On admission to hospital, the patient was afebrile and slightly dehydrated. No focus of infection could be detected. One-third strength physiological saline, 300 c.cm., was administered subcutaneously. Seven hours later the child was reported to have vomited on four occasions. When seen, she had sunken eyes, a moist tongue and pink lips. She was sweating profusely, and showed signs of early peripheral circulatory failure.

Intravenous therapy was commenced with 50 c.cm of a 25% solution of albumin and 200 c.cm. of physiological saline followed by 500 c.cm. of one-fifth strength physiological saline over the next eight hours. Clinical improvement was rapid. Serum electrolyte levels on her arrival at hospital (that is, four hours before she vomited and seven hours before intravenous therapy was commenced) were: sodium, 130 mEq/l; chloride, 71 mEq/l.; potassium, 3 mEq/l. Twenty-four hours later the serum electrolyte levels were normal (sodium, 140 mEq/l.; chloride, 99 mEq/l.; potassium, 4·5 mEq/l.).

Further investigations showed an absence of trypsin from the duodenal juice, numerous fat globules in the stools, and the finger print sweat test as described by Shwachman and Gahn (1956) gave strongly positive (+++) results on several occasions.

Thus the diagnosis of fibrocystic disease of the pancreas was confirmed, and the child was discharged from hospital on pancreatin B.P., tetracycline and a maintenance oral dose of four grammes of salt daily in addition to her normal salt intake.

Discussion.

Acute salt depletion in itself is capable of producing acute vascular collapse. However, when 0·5 to 0·75 gramme of sodium chloride per kilogram of body weight is lost, vomiting is apt to ensue (Marriott, 1950). With the onset of vomiting, a pure salt depletion becomes a mixed water and salt depletion with consequent acute reduction of the extracellular fluid volume, which, unless rapidly corrected, soon leads to peripheral vascular collapse, coma and death.

The association of pink lips with peripheral circulatory failure is most unusual. Rendle-Short (1956) also mentions

pinkness of the lips occurring in a case of fibrocystic disease of the pancreas presenting with acute salt depletion. Why this should occur is not clear.

For children with fibrocystic disease of the pancreas suffering from acute salt depletion, physiological saline should be given intravenously immediately. As there is frequently a temporary fall in the total serum protein level associated with acute salt depletion (Ranowski, Winkler and Elkinton, 1946), the administration of albumin in the cases described may have been warranted.

The normal daily sodium chloride requirement is approximately half a gramme per year of age per day up to a total of five grammes (1·0 to 1·5 mEq/kg. per day). Four grammes of sodium chloride are approximately equivalent to one level teaspoonful.

Throughout the warmer months, children suffering from fibrocystic disease of the pancreas should receive this amount of extra salt and up to four times this quantity during heat-wave conditions.

Summary.

To aid in the recognition of and to draw attention to the condition of acute salt depletion in children suffering from fibrocystic disease of the pancreas, two cases are recorded. The clinical picture and treatment are presented, and prophylaxis with the addition of salt to the diet during summer is strongly recommended.

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I wish to thank Dr. T. R. Biggs and Dr. Felix Arden for permission to record the clinical records of these children. I also thank Dr. Charlotte M. Anderson (Melbourne) for her encouragement in the publication of this paper, and Dr. D. C. Fison, Medical Superintendent of the Brisbane Children's Hospital, for the use of the hospital records.

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Reviews.

Histochemical Technique. By W. G. Bruce Casselman; 1959. London: Methuen & Company, Limited. New York: John Wiley & Sons, Limited. 7¾" x 4¾", pp. 208, with illustrations. Price: 18s. (Abroad).

VARIOUS methods are used for the purpose of studying the chemical structure of living cells and the distribution within the cell of various elements, compounds and enzymes. This study has been called "histochemistry". A small book of 205 pages, entitled "Histochemical Technique", has been brought out in Methuen's "Monographs on Biological Subjects" by W. G. Bruce Casselman. After sections on the meaning and objects of microscopical histochemistry and histochemical analysis and on the preparation of tissues for analysis, sections deal with the detection and localization of lipids, carbohydrates, nucleic acids, proteins, calcium, iron and certain enzymes. The details of the methods are in some cases given in considerable detail; however, in many cases only outlines are given, but there is a very detailed bibliography. Where possible the chemistry of the reaction is given.

This is an excellent book for a beginner in this field of research, and the bibliography enables the reader to delve as deeply as he needs in any particular tchnique. It is a book for the specialist researcher and would have little appeal to the physician or general pathologist. For its particular field it can be highly recommended.

Pulmonary Circulation: An International Symposium, 1958. Sponsored by the Chicago Heart Association. Edited by Wright R. Adams, M.D., and Ilza Veith, Ph.D.; 1959. New York and London: Grune & Stratton, Inc. 10" x 6¾", pp. 336, with many illustrations. Price: $4.50.

IN the proceedings of this symposium, 30 articles by leading American, British and Scandinavian workers consider the recent developments in work on the pulmonary circulation. The papers have been arranged under six broad sections. The first section analyses the historical development of concepts about the pulmonary circulation. In the second section some of the physiological advances are considered, including pulmonary pressure-flow relationships, measurement of phasic pulmonary capillary blood flow, problems of gaseous diffusion and local and reflex responses of the pulmonary blood vessels. The third section deals with structural changes in the pulmonary and bronchial vascular bed in heart and lung disease. The last three sections review the hæmodynamic changes in the pulmonary circulation in primary lung disease, congenital heart disease and acquired heart disease.

There is relatively little material in this book that is new, and most of the work has been presented in the form of original papers during the last few years. At the same time, the presentation of the material has gained in clarity by being in review form. The particular value of this symposium lies in the fact that it emphasizes the areas of real progress in the field and at the same time underlines the areas of remaining doubts and uncertainties. It discusses many important topics, including the measurement of changes in pulmonary vasomotor tone from changes in calculated vascular resistance, and the influence of changes in transmural pressure on these calculations. There is also considerable discussion about the fundamental nature of the pulmonary vasoconstrictor mechanism in pulmonary hypertension.

The problems of the pulmonary circulation are today of outstanding practical interest in the clinical investigation of congenital and acquired heart disease. The specialist in the field will find careful study of this book well worthwhile.

The Child's World. By Phillis Hostler, 1959. Mitcham, Victoria: Penguin Books. 7" x 4", pp. 205. Price: 4s.

HERE is a cheap edition of a delightful book about children, which first appeared in a larger edition in 1953. The author started her career as a teacher, became interested in child development and gradually expanded her knowledge and experience in this field. The book is essentially one for parents, the kind of book many parents are seeking when they ask their doctor for the name of a suitable book after consulting him about some phase of child development or a behaviour problem. No attempt is made to discuss child development in a systematic way; rather, interesting and, for parents, important aspects of children's behaviour and management are discussed in detail.

The book is divided into three parts, the titles of the sections being "The Child in the World", "The Child in the Home", "The Child in Himself"; these, however, do not adequately describe the contents of each part. The first chapter deals with discipline, and the change in community attitudes towards children and in the kind of self-control and community behaviour expected by the community over the past half century. This is not done in an historical chronological way, but examples of attitudes at the parent-child level are given. Chapters follow on punishment, behaviour in company and so on, showing the child as seen by others. The second section is concerned with the child in the family, the development of the mother-child relationship and some of the factors that can influence this. Each succeeding chapter then deals with the next phase of the child's life—the intrusion of the father, of siblings, and later of the schoolteacher. In the third section there are chapters on the primary

emotion, fear, and its bedfellows rage and aggression, on jealousy and on courage.

It is obvious that the author is on the side of children. Her most strenuous efforts are directed towards trying to present the child's point of view, with explanations of why the two-year-old should be afraid when a large Airedale jumps up and licks his face. A feature about the book that should appeal to parents, and especially to mothers, is the author's suggestion of phrases for mothers to use in specific situations. For example, although a mother may feel that her child has been too hard-pressed by the teacher, she should endeavour to remain neutral in front of the child and certainly not belittle the teacher, who has an important role to play in the child's life. "Perhaps Miss Blank didn't understand what you said", "Perhaps you could have done better if you had tried", are replies that nip complaints in the bud and do not undermine the child's respect for his teacher. Similarly, in the handling of aggression against the parent, the mother who has never learned maturer ways of handling her own aggression will promptly strike the child back, saying: "That'll teach you not to hit people." As the author points out, it teaches the exact opposite—violence is the only way to solve difficulties.

This book can be confidently recommended to parents, and the doctor himself can learn a great deal about the child from it also.

Bone Tumors. By Louis Lichtenstein, M.D.; Second Edition; 1959. St. Louis: The C. V. Mosby Company; Melbourne: W. Ramsay (Surgical) Limited. 10¼" × 6¼", pp. 402, with 220 illustrations. Price: £6 12s.

THE new edition of this book is appreciably larger than the first edition. Almost every chapter has been expanded, and one of the most welcome extensions is an amplification of the appendix dealing with some non-neoplastic lesions of bone which may be mistaken for tumours. There is a new chapter on tumours of periosteal origin, and a discussion on tumours of synovium, bursæ and tendon sheaths has been added as an appendix. Another new chapter is devoted to general remarks on the clinical management of bone lesions that may turn out to be tumours. There is good advice here for both the clinician and the pathologist. The author stresses that the clinical, the radiographic and the pathological data must all be taken into account before a bone lesion is treated. Only in this way can one apply the correct treatment and avoid the disaster of treating a benign lesion as malignant. The blind treatment of a lesion diagnosed solely on radiographic appearances is regarded as most reprehensible. In accordance with these views, there are numerous excellent illustrations, both radiographic and pathological, together with a fairly full clinical description of each tumour.

The author has left us still unconvinced that osteoid osteoma is a neoplasm. Nor is the lesion he designates benign osteoblastoma clearly neoplastic.

It was stated in the first edition, and repeated in the second, that osteoclastoma is rare in persons aged less than 20 years. Nevertheless, in the material of one large Australian hospital there have been 25 tumours of this type in the past 10 years, of which 12 were in persons aged less than 20 years. These, however, are minor criticisms, and many pathologists and clinicians have cause to be grateful to Lichtenstein for this book.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Role of Hospitals in Ambulatory and Domiciliary Medical Care", Second Report of the Expert Committee on Organization of Medical Care; World Health Organization. Technical Report Series, No. 176; 1959. Geneva: World Health Organization. 9¼" × 6¼", pp. 32. Price: 1s. 9d. (English).

The findings of a committee which met in March, 1959.

"The Child with a Handicap: A Team Approach to his Care and Guidance", edited by Edgar E. Martmer, M.D.; 1959. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 435, with illustrations. Price: 82s. 6d. (English).

The 27 contibutors are all medically qualified, but the book is intended for the general public as well as medical readers.

"Hémostase spontanée, thrombose et coagulation sanguine"; 1957. Pise: Omnia Medica Éditeur, pp. 214. Price not stated.

Proceedings of the Second Symposium of the Fondation Valentino, Baldacci, 1957. Mostly in French.

"Systemic Lupus Erythematosus", edited by G. Baehr, M.D., and P. Klemperer, M.D.; 1959. New York, London: Grune & Stratton. 10" × 6¾", pp. 84, with illustrations. Price: $3.75.

A Mount Sinai Hospital Monograph.

"Lo Svuotamento Anomalo Delle Vene Pelmonari", by A. Constantini and E. Dall'Aglio, 1957. Pisa: Edizioni Omnia Medica. 9¾" × 6¾", pp. 189, with 56 illustrations. Price not stated.

Entirely in Italian.

"Diabetic Manual", by Elliott P. Joslin, M.D., Sc.D., Tenth Edition; 1959. Philadelphia: Lea & Febiger. Sydney: Angus and Robertson, Limited. 7¾" × 5", pp. 304, with many illustrations. Price: 41s. 3d.

A practical manual for diabetics.

"Grundif der Bakteriologie und Serologie: fur medizinisch technische Assistentinnen", by H. Heinrich; 1959. Jena: Veb Gustav Fischer Verlag. 9¾" × 6¾", pp. 147, with illustrations. Price: 18.70 DM.

Entirely in German.

"Recent Progress in Microbiology", edited by G. Tunevall; 1959. Oxford: Blackwell Scientific Publications. 9¾" × 6", pp. 453, with illustrations. Price: 70s. (English).

Symposia held at the seventh International Congress for Microbiology, Stockholm, 1958.

"Automatic Ventilation of the Lungs", by William W. Mushin, M.A., M.B., B.S., F.F.A.R.C.S., L. Rendell-Baker, M.B., B.S., F.F.A.R.C.S., and Peter W. Thompson, B.A., M.B., B.Chir., F.F.A.R.C.S.; 1959. Oxford: Blackwell Scientific Publications. 8¾" × 5¾", pp. 365, with 190 illustrations. Price: 47s. 6d. (English).

Addressed primarily to anæsthetists.

"The Year Book of Ophthalmology (1958-1959 Year Book Series)", edited by Derrick Vail, B.A., M.D., D.Oph. (Oxon.), F.A.C.S., F.R.C.S. (Hon.); 1959. Chicago: The Year Book Publishers. Sydney: W. Ramsay (Surgical) Limited. 7¼" × 5", pp. 408, with 78 illustrations. Price: £4 2s. 6d.

One of the Practical Medicine Series of Year Books.

"The Year Book of Dermatology and Syphilology (1958-1959 Year Book Series)", edited by Rudolf L. Baer, M.D. and Victor H. Witten, M.D.; 1959. Chicago: The Year Book Publishers. Sydney: W. Ramsay (Surgical) Limited. 7¼" × 5", pp. 480, with 57 illustrations. Price: £4 13s. 6d.

One of the Practical Medicine Series of Year Books.

"The Year Book of Urology (1958-1959 Year Book Series)", edited by William Wallace Scott, M.D., Ph.D.; 1959. Chicago: The Year Book Publishers. Sydney: W. Ramsay (Surgical) Limited. 7¼" × 5", pp. 368, with 82 illustrations. Price: £4 2s. 6d.

One of the Practical Medicine Series of Year Books.

"The Year Book of Pathology and Clinical Pathology (1958-1959 Year Book Series)", edited by William B. Wartman, B.S., M.D.; 1959. Chicago: The Year Book Publishers. Sydney: W. Ramsay (Surgical) Limited. 7¼" × 5", pp. 504, with 136 illustrations. Price: £4 13s. 6d.

One of the Practical Medicine Series of Year Books.

"The Year Book of Orthopedics and Traumatic Surgery (1958-1959 Year Book Series)", edited by Edward L. Compere, M.D., F.A.C.S., F.I.C.S.; with a section on "Plastic Surgery", edited by Neal Owens, M.D., F.A.C.S., F.I.C.S.; 1959. Chicago: The Year Book Publishers. Sydney: W. Ramsay (Surgical) Limited. 7¼" × 5", pp. 448, with 227 illustrations. Price: £4 2s. 6d.

One of the Practical Medicine Series of Year Books.

"Implantation of Ova: Memoirs of the Society for Endocrinology, Number 6", edited by P. Eckstein; 1959. Cambridge: Cambridge University Press. 9¾" × 7", pp. 104, with illustrations. Price: 30s. (English).

Proceedings of a conference held at the Ciba Foundation, London, on November 27, 1957.

The Medical Journal of Australia

SATURDAY, DECEMBER 26, 1959.

CHARLES DARWIN AND "THE ORIGIN".

IN 1858 Charles Darwin and Alfred Russell Wallace jointly presented to the Linnean Society of London the theory of evolution by natural selection which they had independently formulated through years of investigation, observation and thought. For Darwin this may be said to have been essentially a preliminary communication, and in November, 1859, he set out his ideas and the findings on which they were based rather more fully in his most famous work, *The Origin of Species*, or to give it its full title, *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life.* The centenary year of this remarkable book has been appropriately marked throughout the world by orations, symposia and a variety of celebrations. There is now little to be added to what has already been said. Darwin's observations and theories have left their impress and indeed have exerted a critical influence on the development of scientific thought, and his place is established in the history of science. Looking back over the century we may wonder, with the spurious wisdom of retrospection, at some aspects of the story. Little if anything remains of the violent controversy which began in earnest at the British Association meeting in 1860 and continued for most of the rest of the century. The issue cannot be said to be dead or all the differences to have been reconciled even today, as David Lack[1] has pointed out. Perhaps the differences spring more from speaking at cross purposes than anything else, but their existence should be recognized. However, in the widely overlapping fields of men of science and men of religion, most eyes have long since lost the light of battle. This, we may reasonably believe, is how Darwin would have had it. Another phase of the story was the development of what may be called a philosophy of optimism, a somewhat starry-eyed extension into the social sphere of the idea of progress associated with organic evolution. This attitude, more particularly characteristic of the late nineteenth century, has been somewhat shaken by the events of the first half of the twentieth century, but this does not affect the validity of the biological theory.

Of Darwin himself much has been written, but it may be of interest here to note a medical view of him as presented from a particularly eminent source, the President of the Royal College of Physicians, Sir Robert Platt.[2] Darwin, it appears from his autobiography, gave up the study of medicine, which he found little to his taste, because he was convinced that his father would leave him well enough off to manage without earning his living. The medical student was then directed by his father towards the church, but by the time he took a degree at Cambridge this idea also was dropped. At this stage of things the captain of the *Beagle*, preparing to make a voyage to the other side of the world, offered to share his cabin with a young man who would go on the voyage (unpaid) as a naturalist; and despite parental opposition, Charles Darwin was accepted. A combination of delay in sailing and bad weather helped to depress Charles, and Platt states that he then described two characteristics which were to become typical of his later life, namely, the development of neurotic symptoms and the determination not to let them interfere with what he really wanted to do. He was troubled with palpitation and pain around the heart, and having a smattering of medical knowledge was convinced that he had heart disease. However, he would not consult a doctor, because he fully expected to be told that he must not go on the voyage, and he was resolved to do so at all hazard. The voyage lasted for five years and covered much of South America and the Pacific islands. Platt states that it is clear from Darwin's journal of the voyage that during that time he lacked nothing in courage or endurance, for he made long and hazardous journeys into the interior of South America on horseback. He made extensive observations of natural phenomena of all kinds, the climate, geographical formations, and animal and plant life, and began to ponder the thoughts from which his fame was to spring. Further observation and thought followed, and *The Origin* appeared 23 years after the end of the voyage of the *Beagle*. It was an immediate success, the first edition selling out on the day of publication, and aroused widespread interest. Darwin himself played a surprisingly small part in the subsequent controversy, living out his days in comparative quiet. His other main work, *The Descent of Man*, appeared in 1871, and he died in 1882.

Platt states that Darwin's health was of perpetual concern to himself and his close companions during a large part of his life, and comments:

> To the medical reader it is almost impossible to draw any conclusion but that it was psychologically determined. Darwin became ill in the year after his marriage and during his wife's first pregnancy, and was incapable of sustained work throughout the next two years. His devoted and over-protective wife practically gave up any kind of social life and in a few years they moved out of London to the country refuge at Down where they remained. As Douglas Hubble has said: "The perfect nurse had married the perfect patient." At Down, Darwin led a most regular life, breakfasting alone about 7.45 and working for about an hour and a half between 8 and 9.30. He would then come to the drawing-room for his letters, and if there were any family letters they would be read aloud to him as he lay on the sofa, frequently wrapped in his shawl. From 10.30 till about 12, or a little later, he would work again, but by that time he would consider his work done for the day and would go walking with his dog, wet or fine. He

[1] "Evolutionary Theory and Christian Belief: The Unresolved Conflict", by David Lack, F.R.S., 1957, Methuen, London.

[2] *Med. Hist.*, 1959, 3:87 (April).

suffered very much from dyspepsia and from insomnia and periodically he would go away to some hydropathic establishment for a cure.

Platt gives three reasons for the conclusion that Darwin's illness was largely of a psychological nature. The first is that psychological illnesses often take the form of dyspeptic symptoms. The second is that it is difficult to think of any organic illness which would go on for years without causing complications serious to life or permanently disabling. The third, and most important, is Darwin's own attitude towards his health—his preoccupation with it and his constant reference to it as the universal excuse for his not being able to appear in public, or openly to defend his opinions. A good deal has been made of the weaknesses in Darwin's make-up by some who have been unfavourably disposed to his theories, but the two should not fairly be confused. It is enough to suggest that, on the one hand, his preoccupation with his health and his withdrawal from public life and, on the other, his profound and productive thinking on matters of natural history may be the twin ill-assorted fruits of his comparatively sheltered life. His writings stand or fall by themselves. If we would know the man, there is much to ponder over in the striking little vignette with which Platt closes his sketch: "Darwin was a kind man, loved by his children, nearly all of whom suffered from neurotic symptoms and a preoccupation with invalidism. . . . But they were a happy family of kind, unselfish, and tolerant people, who showed considerable indifference to what the world outside thought about them."

Current Comment.

ROBERT BURNS.

ROBERT BURNS was born two hundred years ago. Our remembrance of him lags a little, for his birthday was on January 25, 1759, but that is no warrant for our letting the old year die and his unsung memory with it. Five years ago the life of Burns was discussed in these columns,[1] especially from the medical aspect, and there is not a great deal to add to this, so far as it concerns Burns' illnesses and disabilities and the cause of his death. Many opinions have been expressed on these matters, especially on the cause of his death, but we are not likely to reach finality on the question. Literary autopsies centuries afterwards are fascinating and popular, but rarely satisfactory. Much of the ground is again traversed in a recent article on Burns by Archibald L. Goodall,[2] but it may be better to turn to two other aspects of the poet's relation to the medical profession discussed by Goodall—reference to illness in his works and relations with doctors regarding his work.

Goodall points out that, unlike Shakespeare, Burns does not much refer to the medicine of his times. In the poem "Death and Dr. Hornbrook" Burns lampoons a certain John Wilson under the name of Hornbrook with humour, forthrightness and not a little vulgarity. Wilson, Goodall states, was "not a doctor at all but a village schoolmaster who kept a grocery store on the side and dabbled in *nostra*". Far from harming Wilson, Burns's poem apparently helped to spread his fame. There are a number of other passages of medical interest here and there in Burns's works, including odd references to his own health and illness; the most notable feature of them appears to be their vivid descriptive quality. Goodall's comment on "this meagre harvest of medical allusions" is interesting: "It shows a man not excessively aware of illness in himself or others but with a knowledge of the jargon and philosophy of medicine characteristic of an educated man."

Burns' contact with members of the medical profession was extensive and close, and to many of them he owed much. His father leased land in Ayr from a Dr. Ferguson, who helped the family financially on several occasions. Dr. John McKenzie became Burns' friend after attending his father on his deathbed and introduced the young poet to influential patrons. Dr. Hamilton of Irvine helped him with the Kilmarnock edition of his poems. Dr. James Gregory of Edinburgh was both his professional attendant and his friend and criticized his poems mercilessly ("he crucifies me", wrote Burns). Another friend was Dr. Robert Watt, who as a youth borrowed books from Burns and, it is suggested, may thereby have been inspired to his subsequent literary career. Many other doctors helped Burns on his literary way, for, as Goodall says, "medicine in those days was a cultured profession". Dr. William Maxwell has been blamed for causing Burns's death. Certainly the treatment he ordered the ailing poet may well have helped to that end but any thought of intentional harm may be dismissed. Any other doctor of the day might have prescribed similarly and Maxwell and Burns were such good friends that Burns gave his youngest son the name of Maxwell. Undoubtedly the least happy of Burns' associations with doctors was that with Dr. James Currie, his self-appointed biographer. Currie met Burns only once and then briefly, and, though he meant well, was ill-equipped for the task he undertook. Indeed, although he was high-minded, he altered his facts to suit his theories, and the result was most unfortunate. In large measure he was responsible for the atmosphere that has lingered around Burns of profligacy and alcoholism. Probably Burns was no worse, although no better, than most men of his day and country, and we may well be content, with Goodall, to let our moral judgement be silenced by Oliver Wendell Holmes:

> Ay! Heaven has set one living man
> Beyond the pedant's tether—
> His wishes, frailties, He may scan
> Who weighs them all together.

SPUTNIK H3.

THE claims of Professor Anna Aslan with reference to her treatment of "old age" by the injection of procaine have recently received considerable attention in the lay Press, and many practitioners will already have been questioned about this by their patients. Both for this reason and because the claims come from a reputable source (Professor Aslan works at the C. I. Parhon Institute of Geriatrics in Bucharest), the validity or otherwise of these claims is a matter of more than casual interest. Seven of Professor Aslan's original papers on the subject have been translated into English, but we have not seen them and there has been little authoritative comment on the subject in the English language medical Press. However, at a meeting organized in London last month (on November 19) Professor Aslan had an opportunity of expounding her views in person, and a report of this meeting has been published in the *British Medical Journal* for November 28, together with a full editorial comment. From these sources several interesting points emerge.

Professor Aslan made a good personal impression as regards her sincerity and enthusiasm. However, the more critical of her listeners evidently considered that the data she presented showed a lack of that critical evaluation which is expected in modern medical studies. That this lack cannot be explained away on the basis of the

[1] MED. J. AUST., 1954, 2: 794 (November 13).
[2] *Scot. med. J.*, 1959, 4: 133 (March).

nature of her lecture is indicated by the *British Medical Journal's* editorial comment: "A study of the clinical reports of the Parhon group makes sad reading for the clinician trained in modern scientific method. There is an almost complete absence of control, and blind trials were never used." The substance used in Professor Aslan's work, though dignified by the mystic symbol "H3", is in fact, as she herself states, simply a buffered 2% solution of procaine with a pH between 4·2 and 5·0. Such a solution can be bought in any chemist's shop and does not have to be imported from Roumania. The *British Medical Journal* points out that among the many uses to which injectable procaine has been put in the past, one of the most valuable was in the treatment of rheumatoid arthritis, but that in the last ten years this therapy has been overshadowed by the introduction of ACTH and the corticosteroids for the same purpose. It is stated that some of Professor Aslan's work is therefore a confirmation of the results of previous investigators as to the value of procaine in the treatment of arthritic and other conditions. However, Professor Aslan also claims improvements in the general physiological processes of her patients which amount to a true rejuvenation, and this is of course what has excited so much interest. We are compelled to agree with the *British Medical Journal* that it is difficult to see how the course of injections described by Professor Aslan could possibly produce the results claimed. Procaine is speedily broken down in the tissues, yet each course consists of 12 injections of 5 ml. each, spread over a period of four weeks; these are repeated with intervals of ten days between courses. Professor Aslan is reported as having stated that similar results cannot be obtained by administering the breakdown products of procaine. We can only say that much more satisfactory proof will be necessary before Professor Aslan's claims can be taken too literally.

STEROID THERAPY IN SKIN DISORDERS.

THE introduction of steroids has had a profound effect on almost all branches of medicine, but perhaps on none more so than in dermatology. The principles of steroid therapy in skin disorders have been recently reviewed in an article by R. B. Stoughton[1] of Western Reserve University, Cleveland. He begins by stating that one of the most useful agents introduced for topical dermatology in the past twenty years has been hydrocortisone, and as an indication of the extent to which this is used, estimates that perhaps 10,000,000 containers of steroids for the topical treatment of skin diseases are being dispensed *per annum* (he is presumably referring to the United States), apart from pills, solutions and suspensions for administration by other routes.

Stoughton states that the topical use of steroids, properly applied, has been of great advantage, and that used in this way they rarely produce systemic side effects. There was at first some doubt as to the extent to which steroids could be absorbed through the skin, but it is now known that hydrocortisone is absorbed through normal skin, and it has been demonstrated that, if the skin is damaged by removing its superficial barrier, up to 75% of the steroid applied externally may pass through the skin. Stoughton points out that skin diseases are controlled but not cured by these compounds. Furthermore, the vast majority of skin diseases cannot easily be adequately controlled by the use of steroids alone. Before any attempt to use steroids can be considered, it is necessary to make a proper diagnosis. He suggests that, contrary to many opinions, the introduction of steroids has complicated rather than simplified the management of dermatoses.

The first consideration in the clinical use of steroids in skin diseases is to determine what diseases are relieved by their use and by what route (oral, intracutaneous, topical) they may be administered to best advantage. Stoughton gives a table in which he attempts to summarize the consensus of opinion on the most useful route of administration in 33 different conditions, with the reservation that for most of these skin diseases other therapeutic measures are as important or even more important in their management. The other main points in Stoughton's article may be summarized as follows. Most skin lesions that respond to topical application of steroids will also respond to oral or intracutaneous injection of a steroid; however, many skin diseases which respond to oral or intracutaneous administration will not respond to topical application. There are some skin lesions which will respond to intracutaneous injection of steroids but not to either oral or topical use. This can be explained on the basis of concentration of the steroid in the area in which it is needed. The concentration needed locally, if attained by systemic administration, will usually lead to severe complications if continued over a prolonged period of time. Intracutaneous injection may lead to local atrophy. Some workers have shown that mild systemic side effects are possible from the topical use of fludrocortisone. However, systemic effects from the topical use of hydrocortisone or prednisolone, even over large areas for long periods of time, are practically non-existent. In general the higher the concentration of steroid at its application site, the more beneficial it will be. Frequently the difference in response between a 1% and a 2·5% concentration of hydrocortisone is not significant enough to justify the added expense. The base in which the steroid is incorporated seems to make some difference in therapeutic effect. In general the bases used are primarily of three types: (*a*) greasy or hydrophobic bases, (*b*) cream or hydrophilic bases, (*c*) lotions. In wet oozing lesions the lotions are more satisfactory, and in intertriginous areas creams or lotions are more satisfactory than the greasy bases. In fact, for most skin lesions the hydrophilic bases seem slightly superior to the hydrophobic ones. Steroids are probably used more frequently in the treatment of eczematous conditions than for all other skin conditions combined. The greatest benefit from the topical use of steroids in eczematous conditions probably is experienced in atopic dermatitis and related diseases, such as infantile eczema, dyshidrosis, housewife's dermatitis and neurodermatitis. The topical use of steroids alone is hardly worth while unless other important therapeutic factors are included in the treatment regimen. The oral administration of steroids in eczematous conditions should be discouraged as much as possible, because these conditions are chronic and recurrent, and their long-term management with orally administered steroids frequently leads to unpleasant, and at times drastic, side effects. Stoughton considers that too many patients are given oral steroid therapy for unjustifiable reasons, among which he mentions the desire to impress with a dramatic initial response, the wish to avoid explaining the details of the disease and the complications of its course and management to the patient (in effect, laziness), and ignorance of other effective methods of controlling the disease. He states that only the most severe, extensive and recalcitrant eczematous eruptions present occasional legitimate ground for the oral administration of steroids. It is apparently debatable whether the topical application of steroids is of any value in the treatment of allergic contact dermatitis, though in severe cases their oral administration has a dramatic effect. Stoughton notes a justifiable growing interest in the intracutaneous injection of steroid suspensions in the treatment of conditions in which the lesions are small and few in number; among conditions mentioned in this context are sarcoidosis, keloid and resistant plaques of discoid lupus erythematosus. He states that orally administered steroids are extremely useful in managing acute urticaria, various drug eruptions, pemphigus vulgaris, pemphigoid and erythema multiforme. This seems a very useful review of the essentials of a subject, knowledge of which has come to many of us in a piecemeal fashion.

[1] *J. Amer. med. Ass.*, 1959, 170:1311 (July 11).

Abstracts from Medical Literature.

RADIOTHERAPY.

Giant Cell Tumour of Bone.

R. C. TUDWAY (*Brit. J. Radiol.*, May, 1959) discusses the problems of treatment of osteoclastoma and deals with 18 cases derived from the Bristol Bone Tumour Registry. The tumours are graded after the method of Lichstenstein, which places them in three groups according to morphology. The grade 3 tumours are the most malignant and should, according to the author, be treated from the outset as sarcomata. The grade 2 tumours are potentially malignant and have a considerable tendency to recur after more limited forms of treatment. All tumours which can be completely removed by surgical means must be so treated, provided that the removal can be carried out without significant disability resulting (e.g., tumour of upper end of fibula). Where there is likely to be significant disability, then the choice between radiotherapy and surgery must be made. In the past, these tumours have been treated by deep X-ray therapy where there is marked differential absorption between bone and soft tissue, and this effect results in a great difference in tumour dose, e.g., if the dose to solid bone is limited to 5000*r*, this results in the soft parts receiving only 2750*r*, which may be adequate only for very radiosensitive tumours. Supervoltage therapy avoids these difficulties. If a nominal dose of 4000*r* is given to the tumour, then the calcified area will still receive only 4500*r* to 5000*r* equivalent energy. Thus the tumour hazards of overdosage (and possible causation of late radiation sarcoma) and underdosage (possible tumour recurrence) are avoided. The benign cases are then discussed. Good results were achieved in 14 of 18 cases; two other patients, one after surgery alone and one after radiotherapy alone, required resection later and one required amputation later; one patient died after amputation for sarcoma.

Malignant Disease of the Antrum.

V. M. DALLEY (*Brit. J. Radiol.*, June, 1959) surveys a total of 172 cases of cancer of the antrum and 43 of the ethmoid treated between 1933 and 1955. The cases are classified anatomically: zygomatic (16), palatine (17), frontal (33), alveolar (55), the remainder being non-classifiable owing to advanced disease or being seen after operation. In regard to treatment, it is considered best that there should be a combined approach by surgery and radiotherapy. Radiotherapy is preferred to be given first as most tumours are extensive; it is easier to treat all the tumour by radiotherapy than to attempt surgical removal first, and it is an advantage to treat by radiotherapy when the blood supply is intact as the response is usually better. As a preliminary, the diagnosis is established by means of a biopsy and a Caldwell-Luc operation, if necessary, and septic teeth are removed. Treatment techniques are discussed. With 250 kV X rays the dose is usually of the order of 4500*r* to 5000*r* in five to six weeks. With 2 MeV radiation, it is often possible to reach 6000*r*. The orbit is treated in all cases; unilateral cataracts have been considered a justifiable sequel of treatment and have occurred in 10 cases. Three of these radiation cataracts have been removed when mature and good central vision has resulted. The five-year results in 130 cases in which the patient had received no previous treatment were as follows: differentiated squamous carcinoma, eight survivors out of 31 patients; undifferentiated squamous carcinoma, 10 out of 36; non-squamous carcinoma, five out of 12; histology not known, three out of eight. This gives a total of 26 survivors out of 87 patients for whom adequate data are available, a five-year survival rate of 30%.

Lymphosarcoma in Children.

S. A. ROSENBERG *et alii* (*New Engl. J. Med.*, September 11, 1958) state that, during the last 30 years, some 1269 patients with lymphosarcoma have been seen at the Memorial Centre, and of this group 69 were below 15 years. The commonest initial manifestation was cervical node enlargement; some 21% presented with abdominal symptoms, and solitary bone lesions occurred in 14% (reticulum cell sarcoma). The authors consider that the judicial use of X-ray therapy continues to be the backbone of treatment; the polyfunctional alkylating agents, alone or combined with adrenal steroids, provide little, if any, extra benefit; the antimetabolic drugs, chiefly the folic acid antagonists, are more useful, but largely in children with a picture of acute leukæmia. In this series the five-year survival rate was 17%, which should justify enthusiasm and optimism in the treatment of lymphosarcoma in children.

Cancer of the Bladder.

M. FRIEDMAN (*Radiology*, August, 1959) reports the results of the treatment of cancer of the bladder by rotation irradiation in a series of 81 cases; in most of these the growth was extensive and advanced. The technique and physical considerations of irradiation are discussed; in the successful cases the doses ranged from 8000*r* to 10,000*r*, in 40 to 60 days. These doses are high, but were dictated by the findings at several cystoscopic examinations with biopsy during treatment and by the frequent finding of residual disease after doses of the order of 7000*r*. The author considers that, to improve the results of irradiation of bladder cancer, the prevalent practice of multiple surgical procedures prior to irradiation will have to be discontinued and irradiation started when the disease is in an earlier phase. The results in this series with two-million volt X rays and a rotation technique, were survival rates of 22% after three years and 13% after five years. The author sums up by stating that in his own experience the central intracavitary source (Walter Reed technique) is superior to supervoltage irradiation in bladder cancer.

RADIOLOGY.

Cystic Disease of the Renal Pyramids.

E. L. RUBIN, J. CROSBIE ROSS AND D. P. B. TURNER (*Brit. J. Radiol.*, July, 1959) describe three cases of sponge kidney which they have observed over several years. Clinically, these patients usually present with a mild, intermittent urinary infection, which is easily controlled but which tends to recur. Hæmaturia is occasionally seen, but the presenting symptoms may be due to the formation of small calculi in the cysts. The general condition is good and the prognosis appears to be satisfactory. The radiological picture is characteristic of the condition, showing cystic spaces (filled with contrast medium) contiguous with most or all of the terminal calyces and is seen on excretion urography but not, as a rule, on retrograde pyelography. The appearance is said to resemble clusters of grapes around each calyx. If stones form, they are situated in the small paracalyceal cysts and, if multiple, they may resemble nephrocalcinosis. Usually, but not always, both kidneys are affected. Cystic disease of the renal pyramids appears to be a developmental aberration characterized by cystic dilatation of the collecting tubules. The condition is believed to be benign and is likely to pass unrecognized unless one of the complications to which it is subject brings it to light. The common complications are infection and the deposition of calcium to form small concretions in the paracalyceal cysts. If the radiological appearance is atypical, it may be suggestive of renal tuberculosis. The radiological picture may also be mistaken for necrosis of the renal papillæ, but this lesion runs an entirely different course from cystic disease of the pyramids; a chronic form of papillary necrosis with remissions and exacerbations extending over a period of several years has, however, been described, and it is important to exclude this condition when the diagnosis of cystic disease of the pyramids is being considered.

Peritendinitis Calcarea in the Hand.

E. R. HITCHCOCK AND L. LANGTON (*J. Fac. Radiol.* (*Lond.*), April, 1959) state that the occurrence of periarticular calcareous deposits associated with pain and impaired movement of the shoulder joint is well known, but that it is less fully appreciated that similar deposits may occur in the region of other joints. They discuss the condition with special reference to the hand. The outstanding clinical features of peritendinitis calcarea are pain, tenderness, and limitation of movement. Other manifestations such as swelling, redness, palpable subcutaneous nodules, pyrexia and a raised sedimentation rate vary according to the part affected and the phase of the disease. While the condition can be strongly suspected on clinical grounds, radiographic examination is necessary to establish the diagnosis by demonstrating localized extra-articular calcium deposition in the soft tissues in the region of a joint. The calcium deposit in peritendinitis calcarae is always located in the region of a joint.

Its density is variable, though in general a faint, ill-defined deposit is seen in acute cases and a dense, well-defined deposit in chronic cases. It is extremely rare for more than one deposit to be seen at any given time. The most characteristic appearance is a rather faint deposit containing irregular areas of more dense calcification, the total extent of the deposit being somewhat ill-defined. Deposits also vary considerably in shape and size, some being rounded and others having linear components suggesting their probable location in collateral ligaments or in tendino-muscular junctions of small muscles of the hand. Diminution in size of the deposit occurs rapidly during the course of treatment. Quite often small areas of denser calcification appear within the shrinking deposit, rendering it more clearly visible. Subsequently, fragmentation occurs and the deposit gradually disappears. The diagnosis in acute cases is usually easy if the condition is kept in mind, providing that the calcium deposit is visible. In the fingers and metacarpo-phalangeal region sesamoid bones can be distinguished by their rounded shape, typical sites, and bony architecture. Accessory ossicles and chip fractures can also be distinguished by their bony trabeculæ, as can post-traumatic myositis or tendinitis ossificans. In gout, calcification may rarely be seen n tophi, but characteristic "punched out" areas of bone destruction are also present adjacent to affected joints, often at many sites. Other conditions in which periarticular calcification in the hand could occur are: hyperparathyroidism and other types of metastatic calcification such as myelomatosis, skeletal carcinomatosis and hypervitaminosis D; Raynaud's syndrome and scleroderma; calcinosis universalis; phleboliths in angiomata; Mafucci's syndrome; certain tumours. The differential diagnosis is discussed in each case.

Mediastinal Bronchogenic Cysts.

J. G. SOWERBUTTS (*J. Fac. Radiol. (London)*, July, 1959) records five cases of mediastinal bronchogenic cysts. He describes their radiological appearances and discusses their possible modes of origin. The radiological findings in this series were remarkably constant and similar to those described by other authors. The cysts were seen as clearly defined lesions of homogeneous density lying just below and adjacent to the carina in postero-anterior radiographs, in four of the five cases projecting to the right, where they overlapped the right hilar shadow, extending laterally for a distance of two to three inches from the midline. When penetrated views or tomographs were taken, no splaying or displacement of the carina was recognized. In the films of normal penetration, that portion of the cyst visible to the right of the spinal shadow appeared as a "small arc of a large circle". When seen in lateral views, the greater portion of the cyst lay posterior to the bifurcation of the trachea; in most cases two-thirds lay behind and one-third anterior to the bifurcation. As would be expected from the pathological description, calcification was not seen in any of the cases in this series. In the remaining case the cyst could not be seen on the postero-anterior chest film, but was clearly visible in the right lateral and right anterior oblique views. Barium swallow X-ray examination was carried out in three of the five cases and showed a slight displacement of the œsophagus backwards and to the left. With fluoroscopy no alteration in the size or shape was recognized during the different phases of respiration, swallowing, or on change of position. No air-fluid levels were seen in these cysts, in contrast to intrapulmonary bronchogenic cysts in which this finding is common. The differential diagnosis is discussed, and the following lesions are considered: dermoid cysts, gastro-enterogenous cysts, thymomas, pericardial cysts, enlargement of lymph glands, neurogenic tumours and bronchogenic neoplasms.

Calvé's Disease: Does it Exist?

I. FÉNYES AND L. ZOLTÁN (*Brit. J. Radiol.*, June, 1959) present the case of a boy, aged three-and-a-half years, in whom a vertebral change identical to that of so-called Calvé's disease was detected by radiography at the level of the sixth thoracic vertebra. Laminectomy was performed because of flaccid paraplegia, and biopsy verified that the changes were caused by tuberculous spondylitis. The authors also give an extensive review of the literature and present a table of many cases, reports of which have been published, in which the vertebral changes specified by Calvé were due to disease of the widest variety of ætiology. The authors believe: (i) that the radiographic criteria described by Calvé (1925) can no longer be said to allow a clear-cut differentiation from tuberculous spondylitis; (ii) that the so-called "true" cases of Calvé's disease recorded in the literature may possibly have been caused by tubercle bacilli of low virulence; (iii) that the vertebral change described by Calvé has no pathognomonic significance, it being merely a "roentgen symptom" or, at the most, a "roentgen syndrome"; (iv) that the existence of "Calvé's disease" in the sense of an ætiologically, clinically and radiologically well defined disease, cannot be admitted.

Fracture of the Intercondylar Eminence of the Tibia.

M. H. MEYERS AND F. M. MCKEEVER (*J. Bone Jt Surg.*, March, 1959) state that fracture of the intercondylar eminence of the tibia, although not a common fracture, occurs more frequently in children than in adults. Its greatest incidence is between the ages of eight and 13 years. In children this fracture occurs as an isolated injury without damage to the other supporting ligaments or gliding surfaces of the knee joint; the prognosis for complete recovery without sequelæ is excellent. In adults the fracture is so often accompanied by serious injury to the supporting structures of the knee or other bone injury that serious permanent disability often results. Fractures of the intercondylar eminence of the tibia in children may be divided into three types as demonstrated by skiagrams: Type I, in which there is no dislodgement of the fragment from its bed of origin; Type II, in which there is partial dislodgement of the fragment, but still good apposition of a large portion of the avulsed fragment; and Type III, in which there is complete dislodgement of the avulsed fragment from its bed and no bone apposition of the fragment. Type I and Type II fractures of the intercondylar eminence of the tibia require only immobilization for a length of time adequate to allow bone union, and open reduction is not indicated. Type III fracture of the intercondylar eminence of the tibia with complete dislodgement of the fragment requires open reduction followed by immobilization. If retention is necessary, a simple absorbable suture passed through the thin edge of the avulsed fragment and through the meniscus near its sharp margin with a cutting needle will give adequate fixation. The authors mention six patients treated by open reduction in this fashion, all with excellent results.

Unilateral Exophthalmos.

L. J. BULLOCK AND R. J. REEVES (*Amer. J. Roentgenol.*, August, 1959) discuss 138 cases of unilateral exophthalmos, in many of which X-ray examination offered the only means short of surgical exploration of determining the cause. The X-ray appearance was practically diagnostic in nearly one-third of the cases, and in an additional one-third the diagnosis could be made with reasonable certainty when the complete clinical information was available. Fronto-ethmoidal mucocele was the most common cause of unilateral exophthalmos. The radiographic changes are among the most nearly characteristic of any of the lesions causing unilateral exophthalmos. Fully developed, these consist of decreases in the normal septation of the sinus, loss of the density and pattern of the lining membrane and rounding out of the sinus or apparent expansion. Usually the mucocele occurs in an area of sclerotic bone, the result of chronic infection, although the mucocele itself causes decalcification where it is in contact with bone. A soft tissue mass may be seen, but if there is bone erosion the increased density of the mass may be balanced by the loss of density due to the erosion of bone. A frequent finding when the condition causes exophthalmos is flattening, pushing down, or an actual defect in the orbital margin. The lamina papyracea may be visible bulging into the orbit. Second only in frequency to mucocele as causes of unilateral exophthalmos were periorbital cellulitis and retrobulbar abscess. In this situation the X-ray findings are usually limited to evidence of soft tissue swelling. Clouding, mucosal thickening, or other signs of paranasal sinusitis are often seen since both abscess and cellulitis are frequently complications of sinusitis. Retrobulbar cellulitis secondary to fronto-ethmoid sinusitis occasionally shows destruction or decalcification of the medial orbital wall along with clouding and opacification of the sinus. However, the findings are not indicative and must be interpreted in the light of the clinical findings. Among the malignant neoplasms causing exophthalmos, the most common are those which originate in the paranasal sinuses and consist microscopically of lympho-epithelioma, squamous cell and anaplastic carcinoma, and neuroblastoma.

British Medical Association.

NEW SOUTH WALES BRANCH: NEWS.

We have been asked by the Deputy Medical Secretary of the New South Wales Branch of the British Medical Association to publish the following letter.

135 Macquarie Street,
Sydney.
19th November, 1959.

Dr. Hugh Hunter,
Assistant Secretary,
British Medical Association,
135 Macquarie Street,
Sydney.

Dear Dr. Hunter,

With reference to the matter of the nasopharyngeal radon applicator about which you spoke to me, I think it is unfortunate that this matter has been discussed both in the lay and medical Press. In the article that appeared in one of the evening newspapers, a great many of the statements made were actually the opposite of the truth.

This applicator was first made during the war and I was one of those who were instrumental in having it made for the U.S. Armed Forces, at the request of the E.N.T. Surgeon attached to the U.S. Army Hospital, located at Royal Prince Alfred Hospital. It was provided, at that time, to treat U.S. Air Force fighter pilots, who were unable to fly at high altitudes because of excess lymphoid tissue in the nasopharynx.

It is a different matter of treatment which is under discussion now. It is now a question of the treatment of a non-malignant condition in young children by the use of a very large radioactive source in the nasopharynx; and I am afraid that the consensus of opinion by world authorities is that this is a dangerous procedure and should not be used. As a matter of fact the decision of the Radiological Advisory Council was made after long consideration of the opinions of various authorities and a discussion with the President and Honorary Secretary of the Oto-Laryngological Society. The matter has also been considered by the National Health and Medical Research Council and its Committees.

It is further true that Sydney is the only major city in Australia where the method has been used to any extent. It is interesting to note that the Johns Hopkins Hospital, Baltimore, U.S.A., where the method originated, no longer uses it.

The amount of radon in the applicator was originally of the order of 750 millicuries, and this has latterly been reduced to approximately 300 millicuries, still a very large amount; and even with this amount, the air transport regulations under the *Radioactive Substances Act* have necessitated it being carried in a large container weighing some 90 lbs. for the safety of the personnel handling it. The dose in the immediate vicinity of the applicator is of the order of some thousands of *r*; and I would not be happy to use it myself in a number of children in one session.

The hazards of this treatment which have been called "non-existent" can be divided into:

(1) *Effects on patients.*
  (*a*) Possible interference with growth of bone.
  (*b*) Radiation-induced cancer.
  (*c*) Possible genetic effects.

(2) *Exposure of Staff* in handling a large radioactive source with possible genetic and somatic effects.

The use of radiotherapy in non-malignant conditions in children and people in reproductive period is now, by general agreement, being severely restricted; and radiotherapists are now accepting the decision that many procedures they formerly used are no longer advisable. Even radioactive iodine, which provides a very convenient and successful method of treatment of thyrotoxicosis, is not used in patients less than 45 years of age.

It is true that the radon applicator successfully deals with the exuberant lymphoid tissue in the nasopharynx; but it is thought that other methods should be used in the vast majority of cases. X-ray therapy has also been used in this regard, and although it is much safer than the radon applicator, it is still not without its hazards.

Yours sincerely,

(Signed) HAROLD J. HAM.

Congresses.

CONFERENCE ON CLINICAL ASPECTS OF RADIATION INJURY AND TRANSPLANTATION OF BONE MARROW AND OTHER ORGANS.

FOR some years a series of bone-marrow conferences have been held in Eastern U.S.A., concerning fundamental and clinical aspects of radiation protection and recovery, one of the most fascinating fields of science today. The National Institutes of Health at Bethesda were the site of the Conference on Clinical Aspects of Radiation Injury and Transplantation of Bone Marrow and Other Organs held on September 18 and 19, 1959, and the clinical aspect was well to the fore at this meeting.

Dr. Charles Zubrod, of the Clinical Centre of the National Institutes of Health, introduced the session given to chemical protection against radiation and alkylating agents. Dr. D. G. Doherty, of Oak Ridge National Laboratory, the discoverer of the protection agent AET (S, 2-aminoisothiuronium BrHBr), said that aqueous solutions of AET should be used at once, for at pH's below 6·5 toxic breakdown products are formed, catalysed by carbon dioxide. Mercaptoethylguanandine (MEG) is the active protecting agent in the biological environment. These protective substances must be present within the organism at the time of irradiation, their action theoretically depending on their ability to react with abnormal ions produced from irradiated water. Margaret Kelly (National Cancer Institute) has not been able to get protection in dogs by using AET, whereas very good protection is obtained in mice and rats. Also, the same degree of protection is obtained against nitrogen mustard as against radiation with APT (S, 3-aminopropylisothiouronium BrHBr). AET with thiotepa, "Myleran" and colchicine gives increased toxicity. Pretreatment with AET does not seem to protect tumours against radiation or an alkylating agent as well as it protects bone marrow or lymphoid or intestinal tissue. Dr. Schlosser of Tulane reported a series of 59 patients treated with AET. A dose of 1·5 to 2·0 grammes is all that can be given to man because of symptoms of intolerance, such as skin rash, dyspnœa, hypotension, chills and fever. Less than 1 gramme was tolerated by 10 patients. At this low dosage it is doubtful whether worthwhile protection action can be obtained. "Seconal" in a dose of 1·5 grains prior to administration alleviates some symptoms. Dr. Bruce Synder (N.I.H.) advised the withholding of food for five to six hours prior to the administration of AET. He used a dosage of 14·6 mg. per kilogram to a total of 750 mg. and given at a rate of 75 mg. per minute. Slowing down the rate of infusion cut down toxic manifestations. Doherty stressed that at the low pH of the stomach AET degenerated quickly, so that it should never be given orally. (In 20 minutes at pH 4·5, 47% of AET has been rearranged.) AET must be in the pure crystalline form, and because it absorbs water must be kept under anhydrous conditions, so AET must be made up for patients immediately prior to administration. David Jacobus, of the Walter Reed Radiobiological Unit, described the initiation of an $800,000 screening programme there for radiation protection drugs analogous to the malaria drug-screening programme of former years. Experimentally it was considered that para-amino-propic-phenone (PAPP) together with AET gave increased survival after lethal irradiation. From Roswell Park Institute it was reported that AET had not been able to be given in large enough doses to protect against systemically administered nitrogen mustard, but that it might give enough protection to prevent dissemination effects from a local dose, the result being an improved therapeutic index.

Dr. Georges Mathé, of the Hôpital Hérold, Paris, said that a follow-up investigation of the Yugoslav patients involved in a serious radiation accident at the end of 1958 showed that cataracts were now appearing. In a follow-up investigation after the Y12 radiation accident, Dr. Andreas, of Oak Ridge Institute of Nuclear Studies, said that some of these patients showed muscle weakness and psychic disturbances, and that their white blood cell and platelet counts were in the low normal range. Captain King said that, in planning for future radiation casualties, a radiation exposure evaluation laboratory was being built at the Naval Medical Center, Washington. The Navy had power reactors afloat, and their number would increase exponentially. As well as conventional monitoring and decontamination, there would be very sensitive units for detecting neutron activation of tissues and the gamma-ray spectrum, as well as low-background counting chambers shielded by pre-1945 armour plate.

There appeared to be a growing clinical awareness that too much had been hoped for in the treatment of acute leukæmia with whole-body radiation. Radiation had hastened the end in the majority of Dr. Andrew's patients treated in relapse. Mathé, on the other hand, reported that he had treated six patients with leukæmia in remission with 800 to 1000 rads. The rationale was that it had not been possible to "sterilize" mice when they had a large number of leukæmic cells. Moreover, there are no complications from degradation products of large numbers of destroyed leukæmic cells. Remission was induced by steroids in the first instance. Radiation was used in later remissions, when these were no longer controlled by 6MP. At least ten billion cells of homologous marrow, matched as to phenotypes as far as possible, were given. Four patients showed restoration of the marrow picture, and two, it was thought, showed transitory evidence of secondary radiation disease. The two who may have shown secondary radiation disease received bone marrow from their mothers, the red-cell phenotype of one host and donor being the same. In this case female "dumb-bells" were seen in the boy's circulating leucocytes for a time following irradiation. The secondary syndrome of digestive symptoms, loss of weight and erythrodermia abated with the disappearance of red cells of the donor phenotype and a rise in the lymphocyte count. However, one patient died from a fungous infection and the other with hepatitis. A relapse of the leukæmia occurred in the remaining two cases after five and six months respectively of complete remission. Mathé emphasized that there is no hurry to give marrow. There is probably a period of one to two weeks to assess the situation.

Dr. W. McFarland, of the Naval Medical Center, reported the use of a 4π ^{60}Co field giving a dose rate of 30*r* per minute in the palliative treatment of patients in the terminal stages. He said that the uniformity of the dose to the whole body was said to be within 5% of the stated dose. Daily doses of 100*r* three times per week to a total of 600*r* in a period of two weeks were given. Two patients given lethal whole-body radiation and bone-marrow therapy with this field (which approximates most closely the conditions of the mice experiments) failed to live long enough for restoration to be observed.

Dr. N. B. Kurnick (Long Beach) based his approach to this matter on the premise that intensive and extensive radiotherapy may give results which less extensive therapy may not achieve. Collection of marrow from all patients who are to undergo intensive radiotherapy or chemotherapy is proceeding. He is also storing marrow from all patients with leukæmia in remission. Dr. Mannick (Cooperstown) reported a successful kidney homotransplant between beagles. A male beagle, Sam, weighing seven kilograms and eight months old, received 1300*r* ^{60}Co whole body radiation. He had daily infusions of blood and platelets from a female beagle. Six billion donor marrow cells were then transferred from the female beagle to Sam on about the fourth post-irradiation day. Clinical and hæmatological recovery from the effects of radiation were observed at about the twenty-fourth day, when a kidney was transplanted from the female to Sam, and one week later Sam's kidneys were removed. He died 50 days after the kidney transplant, there having been evidence of female cells in the peripheral blood up to this time. Lymphoid hypoplasia and poor follicle pattern in the spleen characteristic of secondary disease in the dog were seen at autopsy. The kidney was histologically normal. Dr. Donnal Thomas observed that when 600*r* was the LD_{99} for some dogs, he had obtained survival to 750*r* with platelets and antibiotics. Dr. Merrill (Boston) said that kidney transplantation in the human was a technically feasible operation. Among 13 patients given the kidney of an identical twin, there had been long-term survivors. He discussed the case of siblings of similar blood group, except in one of the 26 antigens tested. Diagnostic skin grafts were exchanged. The diseased sibling's skin was rejected by the normal sibling after 20 days, although the skin transplanted from the normal to the diseased sibling "took'. A second graft in the direction "diseased to normal" resulted in a second set response. Thus the siblings were not chimæras, nor were they twins. It was attempted to induce tolerance with 250*r* whole-body radiation. A kidney was transplanted and was still functioning, despite a tense situation following sunburn when there was a mild facial rash and the skin graft began to flake.

Introducing the session on "germ-free life" Dr. Levenson, from the Walter Reed Hospital, spoke about the germ-free laboratory in the Department of Nuclear Medicine. He said that a series of stainless steel tanks, in essence autoclaves, outfitted with a pair of gloves, housed the animals, which were handled through the gloves on the dry-box principle. Ten day old chicks were selected for a radiation experiment. They were obtained by placing sterilized fertile eggs into the laboratory a day before hatching. Of the hatching 75% were sterile. Sterilization of eggs was difficult, for a compromise had to be obtained between complete sterility and death of the eggs. At 10 days the chicks were placed in a smaller germ-free tank to be transported to irradiation at a dose level of 40*r* per minute, and then transported back into their holding tanks. In White Leghorns, a difference in response of 100*r* between germ-free and ordinary chicks was found at the LD_{50}. Professor Trexlor now had germ-free animals in their tenth to twelfth generations. An experiment was planned to learn how much infection entered into the ætiology of secondary disease, by comparing the evidence of that disease in isologous and homologous chimæras, contrasting the normal and the germ-free animal.

Dr. Gordon, of Notre-Dame, defined the germ-free animal as one free from demonstrable associates and free from responses against such associates. He said that there was a deficiency of their reticulo-endothelial system in regions which were normally in contact with infection—for example, bronchi and gut. Gamma and beta fractions were altered on electrophoresis. Circulating antibodies, other than heterospecific antibodies, were not present. Survival of germ-free animals at higher doses of radiation occurred and they died much later than conventional animals and from profound anæmia. In reply to a question asking whether radiation could cause mutation in bacteria, which could then get round the patient's lowered defences after irradiation, Dr. Hellaender replied that the mutation rate was linear to the energy given, so that the possibility of mutation of pathogens already present to other types was possible. Dr. Ferrebee asked whether there should not be a regimen to clean up irradiated patients' bacteria before they went into germ-free surroundings. Dr. Gordon replied that experimentally *Clostridium* and *Streptococcus fæcalis* were reduced to a very low level by continuous penicillin therapy. Survival was obtained comparable to the germ-free situation. Certainly it had been shown many times in rats and mice that penicillin and streptomycin gave increased survival. The question of prophylactic or non-prophylactic treatment in irradiated patients was a very vexed one. It seemed to be the general feeling that antibiotics should not be used prophylactically. Transfusion of fresh blood and platelets should be given when indicated. It was thought that, if possible, the patient should be free of infection at the commencement of treatment. Attendants should be carefully screened for pathogens. Mr. Snow said that a blanket of sterile air could be brought in a conditioning system to surround the patient; that had been pioneered by English workers. It might achieve a near-sterile situation. However, even with electrostatic precipitation, filters and ultra-violet light, 100% sterility of air could not be produced. Dr. Tocantins (Philadelphia) asked whether it was possible to hyperimmunize the donor against some of those organisms. He was loath to use gamma globulin, because of the fear of infection supervening in the hæmatoma. It might be possible soon to apply the principles of the germ-free laboratory to the surgical and the irradiated patient. Already an attachment to the wound area of a germ-free laboratory, in the form of a light plastic glove, had been attempted. The development now was towards a large plastic bag attached to the wound area, and the surgeon worked through it.

The next bone-marrow conference is to be held early in 1960, and its content is expected to be largely experimental.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

RATIONAL DRESS FOR MEDICAL MEN.[1]

[From the *Australasian Medical Gazette*, February 20, 1897.]

(To the Editor of the *Australasian Medical Gazette*.)

Sir,

It was brought home to me very forcibly today how grievously medical men are held in the Egypt of bondage

[1] From the original in the Mitchell Library, Sydney.

to conventionalism and vain tradition. The cause of it was the not uncommon sight of a buggy containing a doctor and his groom. The thermometer was about 90° in the shade. The groom—fortunate mortal—was clothed in irreproachable white from head to foot, whilst his unhappy master sweltered in the orthodox high hat, white shirt, stiff linen collar, and heavy black coat. The conviction that sustained this self-imposed martyrdom probably was that he was upholding his professional dignity, and proving himself to be not as other men. But how foolish it is! Here we have a climate that is semi-tropical for about half the year. It is a climate also that is enervating in the extreme, and all possible causes of loss of nervous energy should be carefully guarded against. The rational costume for such weather is the lightest Jaeger or cellular underclothing with a suit of duck or khaki. The white shirt with its stiff impermeable front, and avidity to take up and retain moisture is at these times an abomination. And yet the average medical man goes about during the Sydney summer in the same clothes that he would wear in London in winter, and wonders why he feels utterly exhausted at the end of the day.

But the question of rational costume goes deeper than the consideration of personal comfort, important though this be. With our present knowledge of infection and the means of guarding against it, is a doctor justified in wearing for weeks or months a garment which cannot be, or, at least, in actual practice is not disinfected, whatever it may have been brought in contact with? Some medical men do strive conscientiously to keep a special suit for visiting infectious cases, but this does not provide against all contigencies. One has to go often to a case of diphtheria or erysipelas or septic abortion without being warned beforehand what the nature of the case is. Enough poison may be carried away on the sleeves of the coat, which is perhaps a new one, to render its wearer a danger to the next parturient woman he visits. Or he may be the actual vehicle of the scarlatinal infection for which an innocent dairy gets the blame. "Doctor", said a friend and patient who has my interests at heart the other day, "why do you go about in that white jacket? Most people think it so unprofessional and you suffer accordingly."

To which I replied that this was in truth the right and proper professional garb, and that twenty years hence the medical man who went about in an old coat that had never been washed would be shunned like the foul fiend. Whilst we need not discontinue our philippic against tight lacing, high heels, and other vagaries of feminine folly, it would be well both for our own consistency and comfort, and for the welfare of our patients that we should set our own house in order.

I am your etc.

Richard Arthur.

Correspondence.

MEDICAL MATTERS AND THE PRESS.

SIR: It is strange that your correspondents, Douglas Miller, John Dowling, W. Scott Charlton, as neurosurgeons of other hospitals should coincide in their protests against an article in the public Press on Parkinson's disease. It is strange that their protests are made some weeks after the publication of the article. It is strange that no such protests accompanied, for example, the intense publicity surrounding Sir Russell Brock's visit to another hospital. Finally, it is a pity they have been intemperate in criticism of the hospital concerned—unaware, perhaps, that such articles are written by reporters whose employers will publish what is news and occasionally may infringe our own rather elaborate ethical code.

Yours, etc.,

JOHN R. SANDS.

"Craignish,"
185 Macquarie Street,
Sydney.
December 4, 1959.

THE MANAGEMENT OF THE ASTHMATIC CHILD.

SIR: The essay entitled "The Management of the Asthmatic Child" by Dr. Helen Walsh, published in THE MEDICAL JOURNAL OF AUSTRALIA of November 21, 1959, whilst an excellent essay and deserving of hearty congratulations to Dr. Walsh, nevertheless contains several errors and omissions.

Some children have a diathesis (or tendency) towards developing asthma. Other children, although exposed to the same conditions in the same surroundings and circumstances, do not develop asthma, although they all may give the same positive skin reactions to the same proteins and irritants. Experience in the asthma clinic of the School Medical Service confirms the observation that asthma, if a child has the diathesis, only develops when the threshold of sensitivity of the mucous membranes of the upper respiratory tract is lowered, and this lowering of sensitivity is nearly always brought about by pathological changes due to infection by the common cold.

Dr. Walsh's remarks regarding the incidence of asthma in children are, I feel, misleading. Her estimate of 10% of children who are attending one practice as being asthmatic is high, as is 20% of families having at least one child with asthma. In 1958, of 83,312 school children fully examined by school medical officers in New South Wales, 3·2% of the boys and 2·1% of the girls suffered from asthma. In 1957, the figures were: of 69,688 examinations, 2·9% of boys and 2·1% of girls suffered from asthma; and in 1956, there were 86,666 full medical examinations, with 2·9% of boys and 1·9% of girls having asthma.

These figures may not be extremely accurate, as no actual survey of the incidence of asthma in New South Wales has yet been undertaken by the School Medical Service. On the other hand, they do represent the actual number of cases of asthma discovered or brought to the notice of the school medical officers during the course of their examinations of school children, and represent a fair cross section of the school population of the State aged from five to 17 years.

Our experience in the clinic is that the so-called "triggers" or exciting factors that may provoke asthma only do so in the presence of upper respiratory tract infection, of which M. N. Albert[1] in 1955 stated:

> One theory is that infections act purely as non-specific factors in individuals who are sensitive to non-bacterial allergens (extrinsic). They lower the threshold of allergic tolerance so that attacks of asthma are now caused by allergens to which the patient was only slightly sensitive and from which formerly he had no clinical symptoms.

Chobot,[2] in 1957, stated that in 400 asthmatic children infection was present in 85·25%, and Stanley Williams,[3] in 1957, stated: "Asthmatic children are born with a susceptibility to the production of bronchiolar spasm when they get an infection (upper respiratory tract infection) . . ." Gwen Donald,[4] 1957, stated: "These children should be kept away as much as possible from the sources of respiratory infection."

We have found that even the emotional "triggers" for asthma do not provoke an attack, except in the presence of upper respiratory tract infection.

In referring to my article, Dr. Walsh stated that "these children were thus protected from a multiplicity of allergens and from infections and nervous disturbances". That is not so. They were protected only from infections of the upper respiratory tract; they were not removed from so-called allergens, and at all times were allowed any food, pets or flowers in their rooms, if they wished, and unless they developed a cold or other upper respiratory tract infection, none of these extrinsic factors provoked an attack of asthma. The children are rarely, if ever, confined to bed for longer than two weeks at a time, and between times no precautions whatever are taken regarding exposure to the so-called allergens.

Dr. Walsh also stated that approximately 75% of the children treated at our clinic for varying periods from three months to five years showed considerable improvement. I think it can be agreed that the figures quoted in my article show that the vast majority of these children obtained very excellent results, and if we eliminated those who did not continue the treatment for longer than three months, then of the remainder who were under supervision for two years or more, 77·8% either had no attack or only one attack of asthma since treatment began, another 16·2% had no attacks in the last six months, and no child showed no improvement in his condition.

[1] *N.Y. St. J. Med.*, 55: 3101.
[2] *N.Y. St. J. Med.*, 57: 1644.
[3] MED. J. AUST., 1: 782.
[4] MED. J. AUST., 1: 874.

It is realized that Dr. Walsh's article is a summary of various authors concerning asthma, but it is surprising to note that so little attention is directed to the preventive treatment of the condition, and most of her remarks are directed towards the actual treatment of attacks of asthma. The results of any one treatment have not been quoted, and I am surprised that no further comment was made on the very excellent results which were quoted in my article and compare so favourably with any other published figures for the treatment of this condition.

As regards prophylactic treatment, we find there is no need to "toughen up" children. They will toughen themselves up as soon as they are relieved of the threat of asthma. On the other hand, it is agreed that nothing can be achieved unless the full cooperation of both the parent and the child is obtained, and to do this, full detailed discussion is necessary, so that both understand the causes and reasons why the child is getting asthma, and the means whereby this can be first averted and then avoided altogether.

Yours, etc.,

N. S. SOLOMONS,
Deputy Director.

School Medical Service,
86-88 George Street North,
Sydney.
November 30, 1959.

THE PROBLEM OF INJURY AND ACCIDENT.

SIR: There is a growing realization in this country that the problem of injury and accident is growing to a dangerous degree. There is also a realization that the present facilities are inadequate. Injury kills or disables the most active and productive members of the community. The risk of accident in the early age group is greater than the peril of disease. This is particularly so in the case of adolescents. As well as the road toll there are accidents at work and in the home.

In the August issue of *The Journal of Bone and Joint Surgery*, the British Orthopædic Association have published a memorandum to Her Majesty's Government on accident services, 1959. This memorandum, of course, deals with the situation in Great Britain, but is entirely applicable to the situation here in Sydney. This memorandum recalls a previous memorandum on accident services in 1943, and despite the recommendations published then, it noted very few of the proposals had been put into effect. The British Orthopædic Association is convinced that the accident services of Great Britain are inadequate because of four things—failures of organization, failures of staffing, failures of accommodation and failures of surgical training.

1. Failures of organization. This is the defect of diffusing injured patients among hundreds of hospitals. How can every hospital, small or large, deal with every accident problem, not only for first aid but for the whole treatment? There should be a limited number of hospitals in which a full service is provided, and to which, as far as possible, all injured patients are sent. "Serious delay in the treatment of the injured occurs not in the transit to hospital but within the hospital that receives the casualties through poor organization and inadequate facilities."

2. Failures of staffing. There are not enough surgeons with orthopædic training to deal personally with every locomotor injury. Segregation in organized accident units would put available talent to better use. The number and the quality of the junior medical staff has to be increased. Similarly, ancillary staff must be well organized. The injured must not be left in the care of the inexperienced.

3. Failures of hospital accommodation. In most hospitals the number of beds allocated for patients with injuries is unrealistic. They are admitted at the expense of the cases waiting elective admission. The buildings themselves are inadequate for present needs and cannot be made adequate by patching-up.

4. Failures of surgical training. Many young men enter hospital service and general practice poorly trained and with little experience in accident work. Better standards of organization, staffing and accommodation will allow sounder post-graduate teaching in this field.

Recommendation.

Accident services should be organized on a nation-wide scale.

The country should be divided into areas with a comprehensive accident unit based upon an existing general hospital. Peripheral hospitals should form part of the accident service, with the headquarters at a general hospital designated for the purpose. At the hospital designated, the staff structure should be overhauled to ensure full supervision by experienced orthopædic surgeons, and to provide adequate staff of intermediate grade and enrolling interested general practitioners. Hospitals not designated as accident centres should be discouraged from receiving injured patients.

The structure and organization of an accident service accident unit should be a department of a general hospital. Out-patients and in-patients should be in one block, with its own entrance for ambulances. Facilities must be available for reception and immediate treatment, including its own X-ray unit, operating theatre and necessary ancillary services. This accident unit should receive all injured patients. Resuscitation services must be immediately available. It should provide for the continued treatment of all patients with injuries of the locomotor system and of patients with multiple injuries. The continued treatment of patients with injuries of head, chest, abdomen or eyes should be the responsibility of the appropriate specialist department. The unit should be closely linked with centres for the treatment of special surgical conditions—head injuries, facio-maxillary injuries, orthopædic disorders and burns. The unit should be of such size to allow a full 24-hour service with all its ancillary services. The average requirement is between 150 and 250 accident beds per half million of the population, assuming that convalescence beds are available, especially for the elderly.

It has been shown conclusively that injuries of the locomotor system account for three-quarters of all injuries. It is clear that the main responsibility must fall upon orthopædic surgeons, one of whom should be in administrative charge of the accident service. The orthopædic surgeon should confine his responsibility to the treatment of limbs and the spine. The neurosurgeon deals with injuries of the head, the thoracic surgeon deals with injuries of the chest, the abdominal surgeon with abdominal injuries, the plastic surgeon with skin and so on. There must be close collaboration between these various consultants. It is emphasized that it is unrealistic to attempt to train surgeons to be expert in every field of surgery—locomotor, abdominal, uro-genital, cardiac, thoracic, cerebral—or in injuries of every part. The creation of casualty surgeons accepting full responsibility for the treatment of all injuries is an undesirable element.

Junior staffing. Short term service of men being trained in consultant appointments will only fill a small percentage of the post. General practitioners and junior surgical staff will carry considerable responsibility if the services are properly organized. The predominant requirement is integration in a proper team. The unremitting supervision by the consultants and with full facilities for consultation and the exchange of ideas.

Peripheral hospitals will have a vital role, and their equipment and staffing requires much thought. The central unit and the peripheral hospitals form the accident service.

A physician should be available at all times of the day and night on a roster system. He should be experienced in two respects. He must be able to distinguish minor from a potentially serious injury. Thus an apparently minor injury, such as a cut in the hand involving a tendon sheath, should be sent as a matter of urgency to the accident unit. He should be competent to deal with minor injuries himself.

Casualty departments will exist, but will no longer receive accident cases. Rehabilitation, teaching in accident surgery, post-graduate instruction and research will follow naturally in the wake of this organization.

Yours, etc.,

H. R. T. HODGKINSON.

135 Macquarie Street,
Sydney.
December 2, 1959.

LIFE ASSURANCE VERSUS SUPERANNUATION INVESTMENT SCHEME.

SIR: Judging by the comments made about the Australian Dental Association's Superannuation Scheme in the British Medical Association (Victorian Branch) News Letter of September, it would appear that the writer is not fully aware of the fact that the scheme embodies life assurance. Life assurance is used in the scheme when it is needed, and discarded when it is not required, thereby avoiding the payment of high premiums at a time when one's income is diminishing. To my way of thinking this scheme offers

TABLE I.

Age Next Birthday on Joining.	Annual Contribution.	Reducing Temporary Assurance.	Position at End of					Retirement Total at Age 65.
			——	5 Years.	10 Years.	15 Years.	20 Years.	
25	£ 200	£ 8000, reducing by 200 *per annum* to disappear at age 65.	Credit in Fund	£ 1050	£ 2400	£ 4150	£ 6450	£ 25,050
			Assurance cover	7200	6200	5200	4200	
			Death benefit	8250	8600	9350	10,650	
45	200	4000, reducing by 200 *per annum*, to disappear at age 65.	Credit in Fund	1000	2300	3950		6200
			Assurance cover	3200	2200	1200		
			Death benefit	4200	4500	5150		
45	500	4000, reducing by 200 *per annum*, to disappear at age 65.	Credit in Fund	2650	6100	10,550		16,450
			Assurance cover	3200	2200	1200		
			Death benefit	5850	8300	11,750		

economic security to the medical man and places him on a more comparable basis with a man in business.

While one does not choose a medical career entirely for financial benefits, in the days when taxation was low and medical fees were high compared with other services, economic security usually came to the successful medical practitioner. Today this rarely happens, and numbers of general practitioners over 60 years of age are still working 24 hours a day and seven days a week. They cannot afford a day off, or take a holiday without their income ceasing, and indeed paying out large sums to keep their practice alive.

In contrast, an equally successful business man can have his days of golf, fishing, holiday or trip abroad, without loss of income. He has built up an organization which supplies him with an income, despite his lessened active association with his business.

The A.D.A. Scheme, however, has offered a tax-free investment plan combined with life assurance at an unbelievably cheap rate which, I feel sure, will change the whole economic structure of medical practice. A large capital reserve is built up which inflates itself as the pound is deflated, and appreciates as the cost of living rises.

Ordinary life assurance, however, merely returns one's savings plus a small amount of interest in the way of bonuses, and it returns the money in pounds that are worth far less than when they were paid in.

Under the yearly assurance plan included in the A.D.A. Scheme, one can obtain very cheap cover, £8000 for the sum of £11 5s. 7d. for a man of 25 years. The same amount of endowment assurance to draw at 65 would cost £194 per year, so that by using the former type of assurance one is saving £182 *per annum*, which can be invested in the fund.

As the £194 is a concessional income tax deduction and the yield from the investment is also tax free, it is obvious that the scheme provides far greater benefit than any ordinary life assurance.

The scheme must surely be financially sound, because it is already in operation by the Chartered Accountant's Society, and the Law Institute is about to launch its scheme. The E.S. & A. Bank has a 40% interest in Federal Trusts Ltd., a company formed to provide these benefits for all self-employed persons.

In my opinion the British Medical Association should have its own scheme in operation for its members, or at least give fuller support to schemes such as the A.D.A. Provident Fund, instead of eulogizing the value of life assurance, which so obviously fails to provide anything like the advantages of the combined life assurance and tax-free investment plan put forward by the Australian Dental Association, and approved by the Government.

On page 13 of the A.D.A. Provident Fund booklet there are examples of anticipated benefits on a conservative basis of 5½% yield. For those who have not a copy of the booklet, this example will prove my point (Table I).

Yours, etc.,

538 Burke Road, Camberwell, Victoria.
JOHN R. SHARLS.

October 21, 1959.

UNIVERSITY INTELLIGENCE.

SIR: I refer to your announcement of appointments to Foundation Chairs in the Medical School of the University of New South Wales.

At no time have I held, or claimed verbally or in writing to have held, "a grant from the N.S.W. State Cancer Council for social study of cancer patients and a long-term study of the pathology and treatment of cancer of the thyroid gland". This is not to say, however, that generous financial support has not been given annually by the Council to other research projects under my direction.

Yours, etc.,

Department of Surgery, University of New South Wales, Kensington.
F. F. RUNDLE.

December 3, 1959.

HYPOTHERMIA IN CARDIAC SURGERY.

SIR: I would like to comment upon Dr. Victor Hercus's paper, "Hypothermia in Cardiac Surgery" (MED. J. AUST., November 28, 1959).

In the development of cardiac surgery conventional hypothermia played a vital part, but the time has come to place it in its proper perspective. There is little to justify its continued use as a means to obtaining a bloodless field in an open heart.

Dr. Hercus states: "We propose to continue using hypothermia for all patients with pulmonary valvular stenosis or coarctation of the aorta, for 'poor risk' patients with Fallot's tetralogy and atrial septal defects (secundum), until such time as the risk of by-pass techniques becomes the same as hypothermia methods which, at the present time, involve practically no risk at all."

1. Pulmonary vavular stenosis. It is now well established that the outflow tract of the right ventricle is of much greater significance than was formerly thought to be the case. Unless this area can be accurately inspected and, if necessary, resected from the right ventricular side, the surgery is inadequate. This cannot be done under hypothermia.

2. "Poor risk" tetralogy of Fallot. If from this one can infer that hypothermia is used to make a non-cardiac shunt operation a little safer, then there can be no objection. Whereas there are indications for shunt operations in this condition, they are few, and whosoever advises them assumes a grave responsibility. In the radical cure of tetralogy of Fallot, where a bloodless field of 60 to 90 minutes is necessary, conventional hypothermia plays no part.

3. Septum secundum. Most children with septum secundum are asymptomatic, and one can almost guarantee that at the age of twenty, they will still be that way. I wonder if it is right to submit such healthy patients to the following risks: (*a*) failure if the diagnosis has been inaccurate; (*b*) frustration if anomalous veins are present; (*c*) inadequacy when the "secundum" is found to be a "primum"; (*d*) danger always from ventricular fibrillation; (*e*) when all over the world these people are being

reoperated for rerouted cavæ and reopened shunts (both due to the hasty inaccurate insertion of sutures). I think they deserve better methods. There is no haste about them.

Hypothermia has played its part, and modified will continue to do so, but its use as described in the above conditions is surely medical history.

Yours, etc.,

189 Macquarie Street, Sydney.
December 2, 1959.

HARRY WINDSOR.

PURE PULMONARY VALVE STENOSIS.

SIR: I would like to comment upon Dr. M. C. Powell's interesting paper on "Pure Pulmonary Valve Stenosis" (MED. J. AUST., November 28, 1959). There is one aspect of his paper with which I disagree, but I think it is an important one.

Dr. Powell states that "it is not always easy to assess that somewhat nebulous expression 'great improvement'." In the patient who has had no symptoms before operation, that assessment can only be made in terms of millimetres of mercury. I would like to have seen the post-operative studies of right ventricular pressure in all cases.

Dr. Powell has instanced two cases in which there was a very substantial reduction in gradient, and two others in which cyanosis had been reversed. This has likewise been my own experience, but unfortunately not always. It is very disappointing to do an adequate valvotomy under vision and later find that the gradient is still high and the cyanosis has not been reversed. This has more often been my experience.

It has become increasingly obvious over the last year that far too little attention has been paid to the great hypertrophied outflow tract. It has been assumed that this will disappear when the obstruction has been relieved. It does not always do so, and is responsible for the gradient. Anyone who has watched the open beating right ventricle in pure pulmonary valve stenosis, and seen the spasm, failure to relax in diastole and narrow outflow tract (quite different from the appearances seen and felt from the pulmonary artery side), no longer wonders why the gradient does not always drop and the cyanosis does not always revert.

The point I wish to make is this. There is now no place for rapid pulmonary valvotomy through the pulmonary artery under hypothermia. The right ventricle must be opened, the valvotomy done and sufficient hypertrophied muscle resected to produce an adequate outflow tract with no significant gradient.

Yours, etc.,

189 Macquarie Street, Sydney.
December 2, 1959.

HARRY WINDSOR.

Australian Medical Board Proceedings.

QUEENSLAND.

THE following have been registered, pursuant to the provisions of Section 19 (1) (a) (d) of *The Medical Acts*, 1939 to 1955, of Queensland: Thompson, John Michael, M.R.C.S., England, L.R.C.P., London, 1945, M.B., B.S., 1948 (Univ. London), M.C.P.A., 1958; Gregory, Patrick John, M.R.C.S., England, L.R.C.P., London, 1955, D.A., R.C.P., London, R.C.S., England, 1959. MacPherson, James Ramsay, L.R.C.P., L.R.C.S., Edinburgh, L.R.F.P.S., Glasgow, 1951; Denborough, Michael Antony, D.Phil. (Oxon.), 1956, M.R.C.P., London, 1959.

The following has been registered, pursuant to the provisions of Section 19 (1) (a) (c) of *The Medical Acts*, 1939 to 1955, of Queensland: Deal, Cedric William, M.B., B.S., 1958 (Univ. Sydney).

The following additional qualifications have been registered: Esler, Edwin John, M.R.C.O.G., 1959; Patterson, Hamilton Stuart, D.C.H., R.F.P. & S., Glasgow, 1959; Sutherland, John MacKay, M.R.A.C.P., 1958; Jackson, Leonard William Lamont, M.R.A.C.P., 1959; Sullivan, Francis Patrick, D.O., R.C.P., London, R.C.S., England, 1959; Cope, John Brian, M.R.A.C.P., 1959.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 21, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.[2]	Australia.
Acute Rheumatism	1	1	1	..	..	..	..	..	3
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	4	..	4
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	2	..	..	..	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	8(5)	10(7)	2(2)	..	..	1	2	..	23
Diphtheria	..	..	..	1(1)	..	..	..	..	1
Dysentery (Bacillary)	..	..	..	2	..	..	2	..	4
Encephalitis	..	2(2)	..	..	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	68(23)	42(19)	21(1)	33(19)	..	2(2)	1	..	167
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	1	..	1
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	2(2)	..	..	..	..	..	..	2
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	28(22)	..	3	..	..	1	..	32
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	7(5)	23(15)	3(1)	16(15)	..	..	..	..	49
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	3	..	3
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	37(21)	19(12)	16(5)	4(3)	..	1	3	..	80
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.
[2] No case of notifiable disease was reported in the Australian Capital Territory for the week ending November 21, 1959.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

Gynæcology and Obstetrics Refresher Course for Recent Graduates.

A FULL-TIME refresher course in gynæcology and obstetrics, especially designed for graduates about to enter general practice, will commence at the Royal Women's Hospital, Melbourne, on Monday, January 25, 1960, and will continue for two weeks. The first week will consist of lectures and demonstrations on stated subjects, and the second of a daily lecture followed by sessions in the ante-natal clinic and the gynæcological out-patient department.

The fee for this course is £10 10s., payable to the Melbourne Medical Post-Graduate Committee. Commencement of the course depends on receipt of a satisfactory enrolment by January 18.

Notice.

THE CHILDREN'S MEDICAL RESEARCH FOUNDATION OF N.S.W.

THE following is a list of donations to the Children's Medical Research Foundation of N.S.W. received from members of the medical profession in the period November 25 to December 9, 1959.

Dr. Lynn Joseph (further), Dr. Jean Lyle (further), Dr. H. R. Sear (further), Dr. M. R. Morey (further), Dr. Loraine C. Hibbard (further), £10 10s.

Dr. I. S. Edwards (further), Dr. A. V. Day (further), £10.

Dr. and Mrs. J. N. Wilson (further), Dr. Guyon M. Purchas (further), Dr. S. Madirazza (further), Dr. H. N. Merrington (further), Dr. E. H. Rutledge (further), Dr. N. H. Saxby (further), £5 5s.

Dr. R. C. Miller, £3 3s.

Dr. Oscar Rychter (further), £2 2s.

Previously acknowledged: £9889 7s. 10d. Total received to date: £9998 12s. 10d.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

O'Kelly, Liam Nicholas, M.B., B.Ch., 1941 (N. Univ. Ireland), 34 Ross Street, Belmont, New South Wales.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Ballenden, John St. Clair, M.B., B.Ch., 1941 (Univ. Witwatersrand), D.M.R.D., R.C.P. and S, 1953; Dwyer, Francis Norman, M.B., B.S., 1956 (Univ. Sydney); Haszler, Charles, M.D., 1931 (Univ. Budapest) (registered in accordance with the provisions of Section 17 (2B) of the *Medical Practitioners Act*, 1938-1958); Lovric, Ivan, M.B., B.S., 1959 (Univ. Sydney); Singer, Henrik, M.D., 1921 (Univ. Budapest) (registered in accordance with the provisions of Section 17 (2A) of the *Medical Practitioners Act*, 1938-1958).

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Panikkar, Radhakrishnan Narayana, M.B., B.S., 1958 (Univ. Adelaide), Royal Adelaide Hospital, Adelaide.

Beilby, Jack Canavan, M.B., B.S., 1955 (Univ. Adelaide), Jervois Street, Petersborough.

Milencewicz, Witalius, M.B., B.S., 1958 (Univ. Adelaide), 97 South Terrace, Adelaide.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: McDonnell, Desmond Leo, M.B., B.S., 1957 (Univ. Adelaide); Clezy, Trevor Munro, M.B., B.S., 1957 (Univ. Adelaide); Shepherd, Peter Byron, M.B., B.S., 1957 (Univ. Adelaide); Rutter, Margaret Claire, M.B., B.S., 1957 (Univ. Adelaide).

Deaths.

THE following death has been announced:

HUGHES.—Norman William Michael Hughes, on December 11, 1959, at Lane Cove, New South Wales.

Diary for the Month.

1960.

JANUARY 8.—Queensland Branch, B.M.A.: Council Meeting.
JANUARY 8.—Tasmanian Branch, B.M.A.: Branch Council.
JANUARY 12.—New South Wales Branch, B.M.A.: Council Quarterly.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £6 *per annum* within Australia and the British Commonwealth of Nations, and £7 10s. *per annum* within America and foreign countries, payable in advance.

THE MEDICAL JOURNAL OF AUSTRALIA

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CONTENTS

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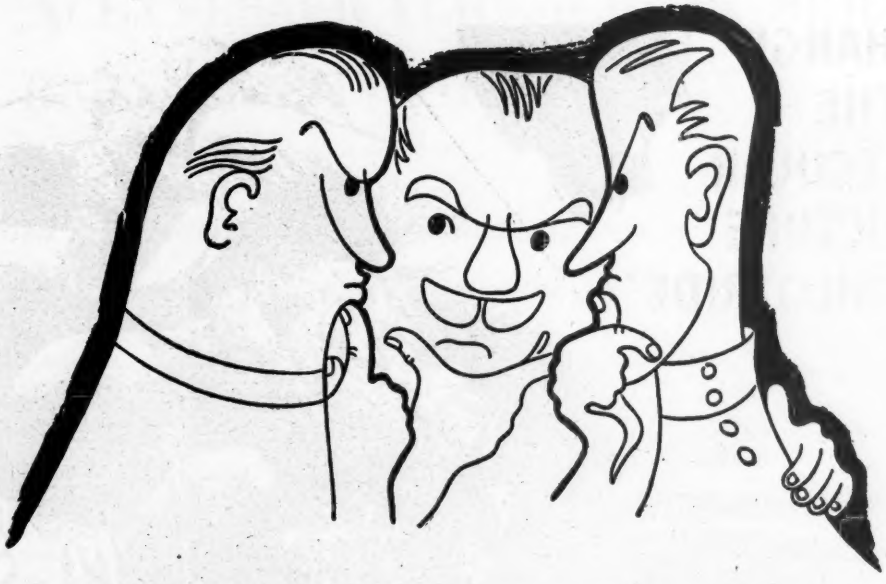

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—Charles Ragan, M.D., "The General Management of Rheumatoid Arthritis," Journal of the American Medical Association, Vol. 141, Page 124, 1949.

"In the treatment of rheumatoid arthritis, do not hesitate to prescribe analgesics. Salicylates are a valuable drug in this condition."

—W. S. Tegner, Brit. J. Phys. Med., 1949, 12, 6.

"Salicylates must take pride of place in any list of pain-relieving drugs for use in rheumatism and arthritis; indeed, in many forms it appears to have a specific action on the pain and sickness."

—W. S. C. Copeman, "Treatment of Rheumatism in General Practice," 1946. (Edward Arnold and Co.)

Each tablet contains:
CALCIUM SUCCINATE, 2.8 GR.,
ACETYLSALICYLIC ACID, 3.7 GR.

Further proof the Bermide formula is superior

A number of facts emerge from a recent study of 233 cases by leading physicians to determine the comparative value of acetylsalicylic acid and a compound of calcium succinate and acetylsalicylic acid—the BERMIDE formula:*

- **It was found that adequate amounts could be administered.**
- **With the succinate-salicylate combination, the relief from pain was greater than that given by salicylates alone.**
- **For the dosage administered there were fewer and milder side effects.**
- **There was no abnormal prolongation of prothrombin time—even after 68 days of administering succinate-salicylate.**

In Arthritic, Rheumatic Therapy

BERMIDE

IS A PROVEN PRODUCT

* **Charles A. Brusch, M.D., Brusch Medical Centre, Cambridge**
George F. Keenan, M.D., Instructor in Orthopædics, Tufts College Medical School.
Arthur F. Sargent, M.D., Instructor in Bone and Joint Diseases, Cambridge City Hospital.
Joseph A. Dorgan, M.D., Instructor in Orthopædics, Tufts College Medical School.
L. A. Grasse, M.D., Staff Physician, Brusch Medical Centre.

Professional sample of BERMIDE and copy of "Index of Arthritic and Rheumatic Therapies" on request.

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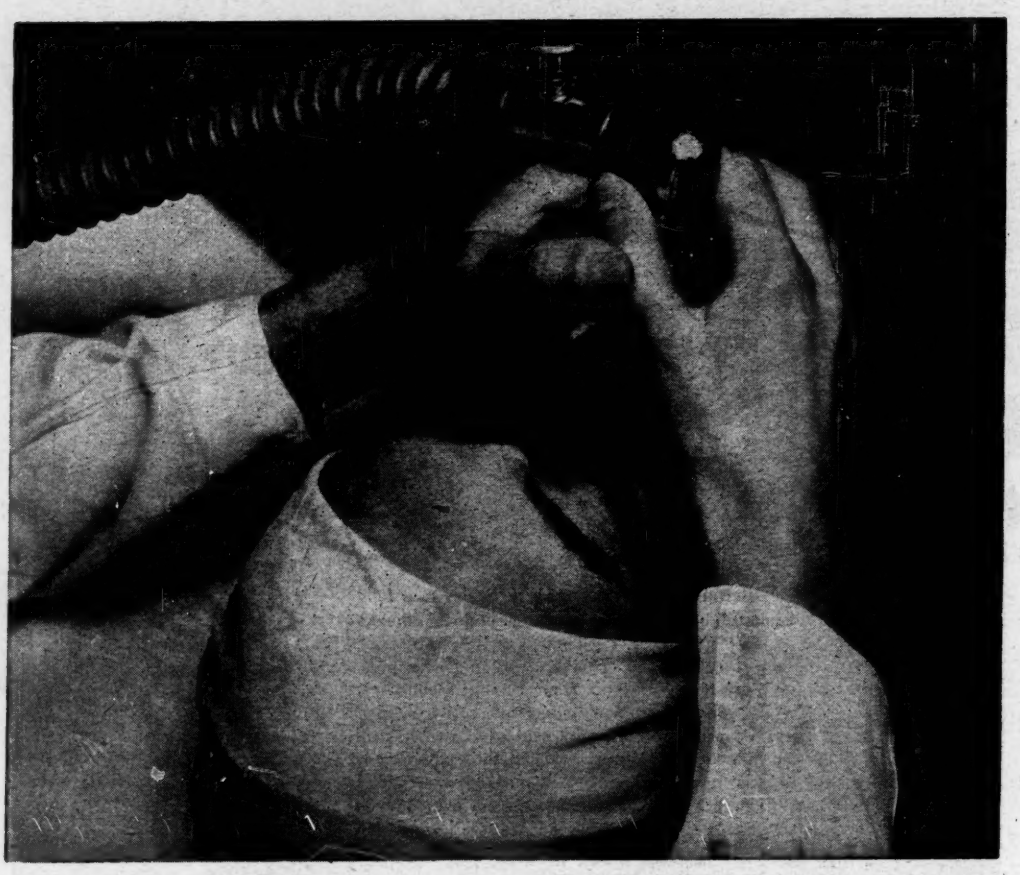
104-108 MOUNT STREET, NORTH SYDNEY



'Fluothane', the new inhalation anaesthetic, has 8 important advantages

The important advantages of 'Fluothane' over other inhalation anaesthetics have been demonstrated in two ways: first by experiment; then in clinical trials covering many thousands of cases, involving patients of all ages undergoing all types of surgical operation.

The special characteristics of 'Fluothane' merit the attention of every practising anaesthetist. They show that this new drug is a most valuable contribution to the greater efficiency and greater safety of modern anaesthesia.

1. *Non-explosive and non-inflammable when mixed in any proportion with oxygen.*
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- ***Bactericidal in a 3-minute scrub***
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GAMOPHEN SOAP (hexachlorophene G.11.2%) is now established as an accepted bland surgical scrub. Harsh alcoholic after-scrub rinses are not necessary, they are in fact contra-indicated. In addition to surgical procedures, routine use of Gamophen should be an added precautionary measure, and should be employed in other vital departments where the risk of cross-infection may originate. Routine use of Gamophen affords maximum cumulative protection by reducing pathogenic skin flora to a minimum.

GAMOPHEN SOAP, ACTIVE INGREDIENT HEXACHLOROPHENE

Tests have shown that the bactericidal action of Gamophen Soap 2% Hexachlorophene is 36% greater against Staphylococcus aureus, Streptococcus hemolyticus and Escherichia coli and 10% greater against Cl. Welchii than is 3½% tincture of iodine.

Gamophen quickly produces a thick, rich lather, every batch is tested for potency.

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ALSO AVAILABLE AS LIQUID SOAP IN ½-GAL. JARS

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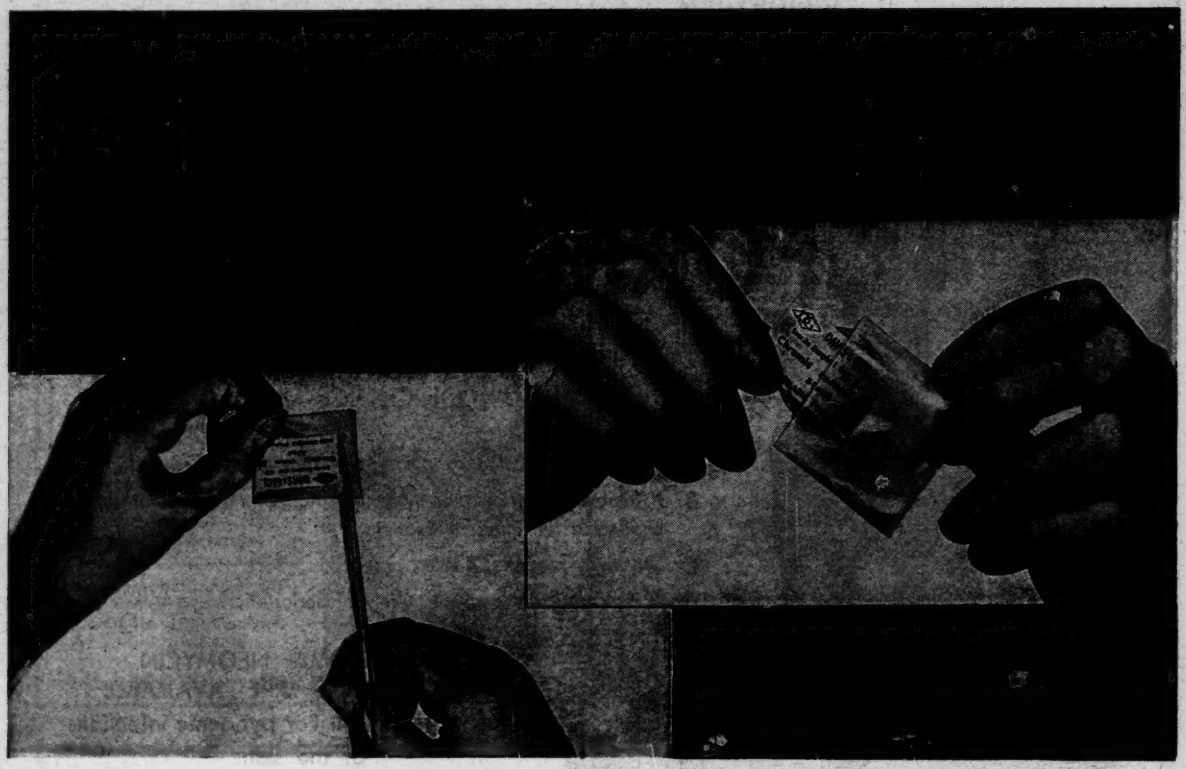

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PRACTICES

CTORIAN MEDICAL PRACTICE.

ere is an excellent opportunity ake over an existing medical tice associated with the Kiewa ro-Electric Scheme in North- Victoria early in the New . Portion of the practice is rwritten, on a per capita ractual basis, with a minimum rantee of £4000 (gross) and, the rest, a quite extensive te practice in the Upper a Valley already exists and be further developed. By ual agreement, the whole of practice is likely to be con- d to one where normal fee- ervice principles apply. Good ital facilities and a well- pped medical centre are avail- and there is no charge for ing.

edical practitioners who may nterested in this unique oppor- ty are invited to write, by ary 11, 1960, to the Secretary he State Electricity Commis- , 22-32 William Street, Mel- rne, or to ring the Commis- 's Medical Officer (62-0241, 279) for further particulars.

R SALE. Western District, Victoria. Half-share two-man pposed, old established practice ntre soldier settlement—new ital, H.E. school, convent— fortable modern house, easy ns. Reply No. 698, c.o. this e.

ELL ESTABLISHED, busy group practice, Sutherland e, Sydney, requires good man replace retiring partner. Prac- conducted from modern block surgeries. Excellent hospital ities available. Arrangements post-graduate leave exist. ly No. 696, c.o. this office.

QUEENSLAND

old Coast. Old established, £7000. Goodwill £3000. Attrac- residence, terms.

arling Downs. Solo, G.T. £6000. dwill £3000. Hospital facilities.

orth Coast. Solo, G.T. £8000. dwill £3000. Hospital facilities.

ountry Town (200 miles Bris- e). G.T. £5000. Goodwill £2500. ndly associations, every lity. Residence, terms.

ssistantships (town and ntry), view partnership, avail-

DAVID W. REID,
Medical Agent,
ICKHAM TERRACE, BRISBANE.

ESIGNING partner's third- hare of Western Suburbs dney) practice. Good hospital ities, surgery and obstetrics. eral time off. Easy terms. T. £18,000. Reply No. 662, c.o. office.

OR SALE. One quarter-share of Newcastle (N.S.W.) prac- £2500. Please address cor- ondence to No. 675, c.o. this e.

OR SALE, A third-share in a Brisbane suburban three-man tice. G.C.T. £19,600. Practice ducted from a lock-up surgery. . £3000. Reply No. 530, c.o. office.

HALF-SHARE AVAILABLE, expanding established 2-man practice. Well organized. Easily worked. Bankstown area, Sydney. Good brick, 3 bedroom house, rent free. Attractive surgery suite. Commence as soon as possible. Reply No. 665, c.o. this office.

ONE-QUARTER SHARE of established 4-man practice in Bankstown District of Sydney. Available for lease or sale. Partner retiring to do post-grad. work. Full hospital facilities. Night and week-end rosters. Reply No. 681, c.o. this office.

LEASE, for one year, from April, 1960, luxury house and well-organized practice in expanding outer Sydney suburb. No obstetrics or surgery. G.C.T. £7000 p.a. Partnership offered on owner's return. Reply No. 690, c.o. this office.

POSITIONS WANTED

PRACTITIONER available for night and week-end locums. Own car. Phone LX3864 (Sydney).

EXPERIENCED general practitioner wishes to make appointments for locum tenens or assistantship work. Has own car and instruments. Town or country. Wide experience in surgery, pædiatrics, obstetrics and gynæcology. Reply No. 683, c.o. this office.

WANTED, by experienced male doctor, aged 31, permanent part-time assistantship, two nights per week and alternate week-ends. In Sydney area. Begin February, 1960. Reply No. 692, c.o. this office.

PART-TIME LOCUM available (two hours a day, five days a week) for three months, April-June, 1960. Experience in diseases of the chest. Reply No. 694, c.o. this office.

CONTINENTAL GRADUATE, 31, married, with hospital experience, completed Sydney University course, seeks assistantship with or without view partnership, within radius of 15 miles G.P.O., Sydney. Reply No. 695, c.o. this office.

LOCUM, M.R.C.O.G., Sydney graduate, available Dec. 28, 3 weeks. Eastern Suburbs, Sydney. Telephone FM 2421, before 9 a.m. or after 6 p.m.

POSITIONS VACANT

LOCUM required, six weeks commencing December 10 1959. for Partnership Practice. Married man, own car. Sixty guineas per week. Reply P.O. Box 114, Queanbeyan, N.S.W.

LOCUM required for 3 weeks, commencing Jan. 1, 1960. Group practice, Fairfield area, Sydney. Salary 45 gns., plus 5 gns. car allowance. Ring UB 1240.

ASSISTANT required for inner suburban Sydney practice, with view. Salary 45 guineas, plus £5 car allowance, £5 living-out allowance and running expenses. Male Australian Protestant preferred. Scope for surgery if desired. Details to Box 1843, G.P.O., Sydney.

MONTAGU MEDICAL UNION, ROSEBERY, TASMANIA.

RESIDENT MEDICAL OFFICER.

Applications are invited for the above appointment.

Guaranteed remuneration £4000 per annum with furnished house at nominal rental.

Small but modern hospital about to be opened, separate medical centre for out-patients under construction. Scope for surgery, obstetrics, anæsthetics, etc.

Applications, stating age, marital state, qualifications and experience, accompanied by copy references, to be addressed to A. J. CREEK, Secretary, Montagu Medical Union, Rosebery, Tasmania.

ASSISTANT, view to early partnership, required in two-man practice, Northern suburb, Sydney. Minimum £3500 p.a. Petrol. Modern flat available to experienced married man interested in medicine. Reply, stating age, experience, to No. 650, c.o. this office.

ASSISTANT WANTED, with view to partnership in six months, for two-man practice 50 miles from Sydney. Very pleasant district, good hospital facilities, attractive suite professional rooms, fully equipped surgery available. Three bedroom house, all electric, septic, rent free. Married man, own car. Salary 45 guineas, £5 car allowance, petrol and oil etc. supplied. Reply No. 613, c.o. this office.

SECRETARY - RECEPTIONIST wanted, 20-25 years old, Macquarie Street, Sydney. Shorthand, typing essential. Apply in writing, No. 702, c.o. this office.

ASSISTANT WANTED in three-man industrial practice, Western Suburbs, Sydney. February, 1960. Salary £2000-£2500 p.a., plus house, plus car running expenses. UY 1613.

ASSISTANT REQUIRED, view partnership, large Sydney group practice. Excellent conditions. Salary £55 per week, plus car allowance of £5. Subsidised accommodation. Reply No. 701, c.o. this office.

LONG-TERM Assistant required, Sydney suburban area. £55 per week. Experienced, capable man required.

Reply No. 697, c.o. this office.

LOCUM, two weeks from Jan. 2, 1960. Prefer with wife or relative to keep house. 45 guineas, plus extra for wife. J. WOOLNOUGH. 35 Oxford St., Epping, Sydney. WM 1933.

LOCUM wanted for 10 wks, from Jan. 18 approx. Car advantage, but not essential. Hosp. appointment and private practice. Western Q'ld. sheep and cattle area. Excellent experience for recent graduate. 45 guineas p.w., plus expenses, or by agreement. Reply No. 651, c.o. this office.

YOUNG married man required as assistant, view 3rd partner within twelve months, for busy outer Western Suburbs practice, Sydney. Accommodation provided. Week-end and night duty roster. Excellent opportunity for keen young G.P. £55 including car allowance. Reply No. 654, c.o. this office.

PUBLIC SERVICE OF TASMANIA.

Applications, addressed to the Public Service Commissioner, Box 123B, G.P.O., Hobart, are invited for the following position to which an appointment will be made in accordance with the provisions of the Public Service Act:

DEPARTMENT OF HEALTH SERVICES.

SCHOOL HEALTH SERVICE.

SCHOOL MEDICAL OFFICER.

Salary Range:

Male. £2213-£2668 per annum, inclusive of cost of living allowance.

Female. £2026-£2481 per annum, inclusive of cost of living allowance (adult female rate).

Duties: To examine school children, advise parents on matters arising from school medical examinations, report on the hygiene of schools and generally assist in the work of the School Health Service. To carry out any other work in the Division of Public Health that may be allotted by the Director.

Qualifications: A medical degree or diploma, registrable in Tasmania, is essential. The Diploma in Public Health will be an advantage; but other applicants should note that Cabinet has approved an arrangement whereby medical officers who have engaged in Public Health work in the Department for two years may be sent, on full salary, to take the D.P.H. course in Sydney, provided that they undertake to return to the Department.

The appointment is whole-time; there is no right of private practice. The appointee will be expected to provide a car, for the use of which on official business a mileage allowance will be paid. The appointment will be made, in the first instance, to Hobart; but the appointee may be required to work in any part of the State.

Applications close at 4 p.m. on January 6, 1960.

MEDICAL DIRECTOR.

Cyanamid of Great Britain seeks a qualified medical practitioner between 35 and 45 years of age to join the organization as Medical Director for Australia and New Zealand on a part-time basis. Travel will total two months a year and headquarters will be Sydney.

Initial salary £2143 a year.

For particulars:

MR. J. T. HOPKINS,
Lederle Laboratories,
800 Princes Highway,
Tempe, N.S.W.

LL 5242. LL 5242.

POSITIONS VACANT—Contd.

GOVERNMENT OF WESTERN AUSTRALIA.

DEPARTMENT OF PUBLIC HEALTH.

NORTH-WEST MEDICAL SERVICE.

Applications are invited from registered medical practitioners to fill positions in the North-West Medical Service of the Department of Public Health.

The following salary and conditions apply.

Salary. £3270 p.a. (inclusive of District Allowance). The sum of £120 p.a. is deducted for rent of a completely furnished residence. A motor vehicle is provided and running costs paid by the Department. One month recreation leave annually.

Further particulars are obtainable from the Commissioner of Public Health, 57 Murray Street, Perth, Western Australia.

WANTED, Locum for 2-man inner suburb (Sydney), lock-up practice, while one partner is away. May-October, 1960. £60 per week. Reply No. 686, c.o. this office.

WANTED, Assistant, British, capable, experienced, energetic. City (Sydney) general practice. Live-in. Excellent conditions. £55 p.w., plus bonus after 12 months' service. Reply No. 678, c.o. this office.

LOCUM wanted for 2 or three weeks from January 18, 1960. Western Suburbs (Sydney). £50 p.w. and allowances. Preferably single. Live in. Reply No. 685, c.o. this office.

ASSISTANT, with view, 3-man practice, Bankstown District, Sydney. £2750 p.a., including car allowance. Reply No. 641, c.o. this office.

GENERAL surgeon, higher degree preferred, invited to join seven-man group with interest in general practice and prospect of taking over major surgery. To start as assistant at £2500 p.a. Ring YU 1348 (Sydney).

OBSTETRICIAN and gynæcologist (Protestant), prepared to share G.P. responsibility, required by well appointed and expanding Melbourne group practice. Salary at £2600 per annum during trial period. Reply No. 627, c.o. this office.

THREE young partners (G.P., surgeon, physician), seeks assistant, view fourth partner. £50 to £60 per week; 3 bedroom house available to rent. G.P. with special interest (medicine, children, eye, E.N.T., anæsthetic, obstetrics, skin, etc.) or specialist in any of the above. (Queensland). Reply No. 679, c.o. this office.

ASSISTANT WANTED, Sydney North Shore, expanding solo practice. Fifty pounds p.w., plus petrol and oil. Reply No. 691, c.o. this office.

ASSISTANT WANTED, Eastern Suburbs, Sydney, medical practice. Salary £3000 p.a. Apply with particulars. Reply No. 645, c.o. this office.

LOCUM WANTED for three-man practice view partnership. Fifty guineas, including car allowance. Lodgings. Mildly tropical coastal city. P.O. Box 328, Rockhampton, Queensland.

LOCUM wanted from January 9 to 23, 1960. Live in. Married. Own car. Outer Sydney suburb. 45 guineas p.w., plus car allowance, plus 8 guineas living allowance. Phone UB 4169.

ASSISTANT, view partnership, required for group practice (3) within 200 miles Sydney. Excellent facilities. Terms £2500 p.a., plus car allowance, comfortable residence. Reply No. 672, c.o. this office.

WANTED, Assistant, view partnership if desired. 50 guineas p.w. and rent-free furnished house. Hurstville area, Sydney. Reply No. 556, c.o. this office.

HOSPITAL APPOINTMENTS

THE BROKEN HILL AND DISTRICT HOSPITAL,
P.O. BOX 457,
BROKEN HILL, N.S.W.

Applications are invited from 2nd year Resident Medical Officers (male or female) for position of Resident Medical Officer at Broken Hill and District Hospital.

Salary: £1600 per annum, less £3.11.3 per week for board and lodgings. In the case of married applicants, a furnished rent-free residence is available. Thirty days' annual leave; rail or air fares refunded after 6 months' service.

Duties: Rotating residencies every 3 months in medicine, surgery, casualty; and obstetrics and anæsthetics. Daily average inpatients 265.

Applications, addressed to the undersigned, should state full particulars of qualifications and experience, and enclose copies only of any credentials.

R. H. NANKIVELL,
Secretary-Business Manager.

WARWICK BASE HOSPITAL, QUEENSLAND.

Applications are invited for the position of Junior Resident Medical Officer. Salary range £1399 10s. to £1949 10s., dependent on experience. Board and lodging provided single man, furnished flat available married man. Applications should be addressed to the Secretary giving full details of qualifications, age, experience and marital status.

RICHMOND HOSPITALS BOARD, N.Q.

Applications are invited for the position of Part-Time Medical Superintendent, Richmond Hospital. 21 bed hospital. Daily average 8. Salary range £1300 minimum to £1425 maximum per annum. Free use of large house (unfurnished), also lighting, fuel and power. Township in centre of rich pastoral area and appointee has right of private practice. Submit applications in writing to Secretary, Box 60, P.O., Richmond, Queensland.

DEPARTMENT OF PUBLIC HEALTH, N.S.W.

DIVISION OF PSYCHIATRIC SERVICES.

MEDICAL STAFF.

Applications are invited from medical graduates for the undermentioned positions in New South Wales Mental Hospitals.

MEDICAL OFFICERS.
Salary £1911 range £2311 with progression to £2611.

PSYCHIATRISTS.
Salary £2836.

JUNIOR SPECIALISTS.
Salary £3010.

SPECIALISTS.
Salary £3100.

CLINICAL DIRECTORS.
Salary £3250.

Medical Officers must have a minimum of two years' post-graduate experience.

For the positions of Psychiatrist, Junior Specialist, Specialist, and Clinical Director, applicants must be in possession of a Diploma of Psychological Medicine. Appointment to positions of Junior Specialist, Specialist, and Clinical Director will be considered having regard to an applicant's experience as a psychiatrist. A minimum of three years' experience is required for appointment as Junior Specialist and five years' for Specialist or Clinical Director.

Appointments on resident basis, residences provided at low rentals for married officers, single accommodation available. Four weeks' annual recreation leave, liberal sick leave and extended leave. In some cases, appointments as Junior Specialist, Specialist or Clinical Director will be on a non-resident basis. Leave in these cases will be three weeks per annum. Permanent appointment, subject to medical fitness, with right to contribute to Superannuation Fund, with liberal pension rights.

Vacancies in Mental Hospitals in Sydney Metropolitan Area, and in country districts (at maximum distance from Sydney of 200 miles).

Apply Public Service Board, 19 O'Connell Street, Sydney, by February 6, 1960.

ROYAL HOSPITAL FOR WOMEN, PADDINGTON, NEW SOUTH WALES.

Applications on prescribed form are invited for the positions (2) of Hon. Obstetricians and Gynæcologists. Closing date February 12, 1960, at noon.—W. L. PERRY, Secretary, Benevolent Society of N.S.W., Thomas Street, Sydney.

THE QUEEN VICTORIA MEMORIAL HOSPITAL,
172 LONSDALE ST.,
MELBOURNE.

Applications are invited from legally qualified medical practitioners (female or male), holding higher surgical degree, for appointment as:

ACTING
HONORARY JUNIOR SURGEON.

Duties to commence early in February, 1960, to end of April, 1960.

Closing date: January 30, 1960.

Further information may be obtained on application to the undersigned.

NELL STEPHENSON,
Manager.

ALFRED HOSPIT
COMMERCIAL ROAD,
PRAHRAN, VICTORIA.

The Board of Management Alfred Hospital hereby in applications from legally qual medical practitioners for appo ment of:

ASSISTANT
TO HONORARY NEUROLOG

Applicants should have, or about to obtain, a Senior Me Degree and intend to pu Clinical Neurology or work allied fields, as a career.

Duties will provide an op tunity for original work.

Salary range £1400-£2500 annum, according to qualificat and experience.

Duties are to commence in F ruary, 1960, and appointment be for a period of one year w eligibility for appointment fo further term of one year.

Applications, on forms availa at the hospital, will be received the undersigned until January 1960.

G. B. CANHAM,
Acting Manag

PRINCESS MARGAR
HOSPITAL FOR CHILDR
PERTH, WESTERN AUSTRAL

Applications are invited for post of:

SENIOR
HOSPITAL SURGICAL OFFICE

Salary £2573 per annum (s ject to cost-of-living variatio Minimum term of appointment years. Travelling allowances av able. Post is non-resident.

Applicants must have had su able previous experience and h a higher qualification.

Applications, in writing, wh close on January 15, 1960, sho detail personal particulars, qua fications and experience to da and include the names of t referees.

J. D. CLARKSON,
Manag

TARANAKI HOSPITAL BOAR
NEW ZEALAND.

REGISTRARS.

Applications are invited for t following Registrarships at t New Plymouth Hospital, N Zealand, for 1960:

SURGICAL REGISTRAR.

The New Plymouth Hospital recognized by the Royal Colleg of Surgeons.

MEDICAL REGISTRAR.

This position offers a conside able amount of psychiatric expe ence in addition to a sound trai ing in medicine.

Salary for Junior Registra £960-£1015, for Seniors £107 £1230, with free board and lodgi or a living-out allowance of £2

Good partly-furnished fla available.

Transport expenses from Au tralia to New Zealand will be m subject to an undertaking remain in the employ of the Boa for not less than one year.

Applications to be addressed and further particulars may obtained from The Medical Supe intendent, New Plymouth Hospit New Plymouth, New Zealand.

HOSPITAL APPTS.—Continued

PALMERSTON NORTH HOSPITAL BOARD. PALMERSTON NORTH, NEW ZEALAND.

RADIOLOGIST.

Applications are invited from registered medical practitioners for the position of whole-time radiologist in charge of the diagnostic X-ray Department at the Palmerston North Hospital, New Zealand.

Applicants must have had practical experience in Diagnostic radiology and should hold a higher qualification in this specialty in order to qualify either as a Senior or as a Junior Specialist under the Hospital Employment (Medical Officers) Regulations, 1957.

Salary range:

Senior Specialist—
(a) £2650-£2950 per annum.
(b) £2400-£2650 „ „
(c) £2100-£2400 „ „

Junior Specialist—
£1700-£2000 per annum.

(Salaries quoted are in New Zealand currency.)

Conditions of appointment may be obtained on application to the undersigned.

Applications, giving full particulars as to age, qualifications and experience and accompanied by recent testimonials and advice as to the earliest date on which appointment could be taken up, to be addressed to the Secretary, Palmerston North Hospital Board, P.O. Box 607, Palmerston North New Zealand. Applications will close Friday, January 29, 1960.

R. S. WILSON,
Secretary.

ROYAL PERTH HOSPITAL.

RESARCH FELLOW.

Applications are invited from legally qualified medical graduates for the position of Part-Time Research Fellow with the Panel for the study of Neoplastic Disorders of Bone Marrow and Lymphoid Tissue, which has been formed by the Clinical Staff of this hospital and the Princess Margaret Hospital for Children.

Salary £1000 per annum—5 sessions weekly.

The appointment will be tenable initially for one year, and applications should reach the undersigned not later than January 11, 1960.

JOSEPH GRIFFITH,
Administrator.

NAMBOUR HOSPITAL, QUEENSLAND.

Applications are invited for the position of Resident Medical Officer available at above hospital, approximately mid-December, 1959. Daily average inpatients approximately 80, outpatients approximately 50. Salary range, 1st year £1230, 2nd year £1385, 3rd year £1550, plus basic wage adjustment, at present £99 per annum.

Single Officer's quarters available at hospital.

Nambour is the centre of a rich farming area. Seventy miles from Brisbane and 8 miles from popular coastal pleasure resorts. Excellent climate. Wide general experience available to Resident Medical Officers. Applications accompanied by references, particulars of age, experience and marital status to be addressed to Secretary, Maroochy Hospitals Board, Nambour, Queensland.

WELLINGTON HOSPITAL BOARD. WELLINGTON, NEW ZEALAND.

WELLINGTON HOSPITAL.

WHOLE-TIME ANÆSTHETIST.

The Wellington Hospital Board invites immediate applications from registered medical practitioners for a position as Whole-Time Anæsthetist at Wellington Hospital.

Applicants should qualify as Senior or Junior Specialist under the New Zealand Hospital Employment Regulations, 1957, and the salary and grading for the position will be in accordance with these Regulations and subsequent amendments. Senior Specialist Scale (c) £2100-£2400; Junior Specialist £1700-£2000. Salary rates quoted are in New Zealand currency.

Intending applicants should apply to the Trade Commissioner for New Zealand, 14 Martin Place, Sydney, or 428 Collins Street, Melbourne, for a schedule of information regarding this position.

Applications, giving full particulars as to age, qualifications, experience, and stating the earliest date upon which duty can be commenced, should be forwarded immediately to the Secretary, Wellington Hospital Board, Private Bag, Wellington Hospital, Wellington, New Zealand.

A. F. WILTON,
Secretary.

MARLBOROUGH HOSPITAL BOARD, BLENHEIM, NEW ZEALAND.

MEDICAL STAFF.

Applications are invited for a House Surgeon, Senior or Junior, or one of Junior Registrar Status on the staff of the Wairau Hospital, Blenheim, New Zealand, an institution of 190 beds, modern and well equipped in every way; single quarters available. Salary Junior Registrar £960; Senior House Surgeon £870; Junior House Surgeon £760; free living-in; refund of fares subject to the appointee undertaking to remain in the Board's service for one year.

Applications with full particulars should be addressed to the Medical Superintendent.

GEO. MITCHELL,
Secretary.

NORTH BRISBANE HOSPITALS BOARD.

Applications are invited for the position of full-time Medical Superintendent, Southport Hospital (general and maternity). Salary £2650 minimum, £2700 maximum, plus basic wage adjustments, with house, light and fuel. Particulars may be obtained from the General Superintendent, Brisbane Hospital, Herston, Brisbane, and applications supplying full details of age, qualifications and experience should be addressed to the Manager, North Brisbane Hospitals Board, Herston Road, Brisbane, on or before January 9, 1960.

THE QUEEN VICTORIA MEMORIAL HOSPITAL, 172 LONSDALE ST., MELBOURNE.

Applications are invited from legally qualified medical practitioners (female or male) for the following positions:

RESIDENT
ANÆSTHETIC REGISTRAR.

(Applicants to have had at least one year's Anæsthetic experience.)

TWO RESIDENT
PÆDIATRIC REGISTRARS.

(For Children's Ward and Neo-Natal work.)

Salary: £1506.4.0 p.a., plus board and residence.

Duties to commence February 1, 1960.

Applications, on prescribed form, close January 8, 1960.

NELL STEPHENSON,
Manager.

FAIRFIELD DISTRICT HOSPITAL.

MEDICAL STAFF.

The Fairfield District Hospital, Fairfield, N.S.W., invites applications for the following positions on the salaried medical staff:

1. MEDICAL SUPERINTENDENT

Salary range £2200 to £2600 p.a., dependent on qualifications and experience. The successful applicant would be in charge of four Resident Medical Officers, and shall, under the supervision of the Honorary Medical Staff, control the medical work performed by the hospital.

2. SECOND YEAR RESIDENT MEDICAL OFFICER.

Salary approximately £1260 p.a. The hospital has 127 beds and an adjusted daily average of 120. There are 57 Honorary Medical Officers on the staff.

Applications close on January 8, 1960, and the successful applicants would be required to take up duty on or about February 1, 1960.

Further information on either position may be obtained from the undersigned, and application forms are available on request.

J. J. SMITH,
Chief Executive Officer and Secretary.

ATHERTON HOSPITAL.

RESIDENT MEDICAL OFFICER.

Applications are invited for the position of Junior Resident Medical Officer at the Atherton Hospital, North Queensland. Salary classification at present including all Basic Wage adjustments. First Year, £1389; Second Year, £1564; Third Year, £1739; Fourth Year, £1939; to which is added £48 northern allowance.

In consideration of the successful applicant visiting Koombooloomba Clinic fortnightly a subsidy at the rate of £250 per annum will be paid until June, 1960, at least. Transport will be provided or alternatively mileage will be paid for the use of own car at Public Service rates.

A furnished flat is provided to accommodate a married couple with one child. Free Board and Lodging provided for a single person. Daily average, inpatients 80, outpatients 60.

Applications to:

W. H. SHERRIN,
Secretary,
Atherton Hospitals Board,
ATHERTON, N.Q.

HOSPITAL APPTS.—Continued

RENWICK HOSPITAL FOR INFANTS, SUMMER HILL, N.S.W.

Applications, on prescribed form, are invited for the position of Resident Medical Officer from January, 1960. Salary range of £1019 to £1944 p.a., less £3.13.11 p.w. B. and R., subject to basic wage variation. Particulars from Medical Superintendent. Canvassing of Directors is prohibited.—W. L. PERRY, Secretary, Benevolent Society of N.S.W., Thomas Street, Sydney.

THE QUEEN VICTORIA MEMORIAL HOSPITAL, 172 LONSDALE ST., MELBOURNE.

Applications are invited from legally qualified medical practitioners (female or male) for appointment as:

RELIEVING RESIDENT MEDICAL OFFICER FOR OBSTETRICS.

Period of eight months, from beginning of April, 1960.

Salary range: £981.4.0-£1231.4.0 p.a. (according to years of graduation experience), plus board and residence.

Applications, on prescribed form, close January 30, 1960.

NELL STEPHENSON, Manager.

GLADSTONE HOSPITALS BOARD.

RESIDENT MEDICAL OFFICER.

Applications are invited from registered Medical Practitioners for the above-mentioned position at the Gladstone Hospital, Qld.

Salary classification: first year £1350 p.a., second year £1525 p.a., third year £1700 p.a.

The above salaries are subject to Basic Wage adjustment, at present £39 p.a.

Comfortable cottage provided single or married person—free board single appointee.

Appointment terminable by one month notice on either side.

Please forward application, stating age, marital status, qualifications and experience to Secretary, P.O. Box 142, Gladstone, Qld., advising also date available commence duties.

REPATRIATION GENERAL HOSPITAL, GREENSLOPES, BRISBANE, QUEENSLAND.

MEDICAL OFFICERS, GRADE I (RESIDENT).

Applications are invited for the above positions, which are particularly suitable for practitioners interested in obtaining a higher Degree, or wishing to further their hospital experience.

Salary range: £1935-£2375 (actual).

Commencing salary will depend on experience and qualifications.

Applications should be made direct either in writing, or by telephone, to the Senior Medical Officer, Repatriation Department, G.P.O. Box 651-K, Brisbane (telephone 32-0331); or to the Medical Superintendent, Repatriation General Hospital, Grenslopes, Brisbane (telephone 97-1061).

WELLINGTON HOSPITAL BOARD.
WELLINGTON, NEW ZEALAND.

SILVERSTREAM HOSPITAL.

RESIDENT JUNIOR PHYSICIAN.

Immediate applications are invited for the position of Resident Junior Physician at the Silverstream Hospital, Wellington, New Zealand. This is a geriatric hospital and includes some long-stay orthopædic patients.

The position will be designated under the Hospital Employment Regulations as that of a Junior Specialist or a Medical Officer on Special Scale and the position will be subject to grading procedure.

The relevant salary scales are as under:

Junior Specialist, £1700-£2000.

Medical Officer of Special Scale B, £1800-£2000; C, £1500-£1700.

The salary ranges quoted are in New Zealand currency.

Details regarding assistance with transport expenses for the appointee and family are given in the Schedule available. A three bedroomed house is available in the hospital grounds and a rental of £150 per annum is deductible from the salary for the house, including fuel and light.

Intending applicants should apply to the Trade Commissioner for New Zealand, 14 Martin Place, Sydney, or 428 Collins Street, Melbourne, for a Schedule of Information regarding this position.

Applications, giving full particulars as to age, qualifications, experience, and stating the earliest date upon which duty can be commenced, should be forwarded immediately to the Secretary, Wellington Hospital Board, Private Bag, Wellington Hospital, Wellington, New Zealand.

A. F. WILTON, Secretary.

THE QUEEN VICTORIA MEMORIAL HOSPITAL, 172 LONSDALE ST., MELBOURNE.

Applications are invited from suitably qualified medical women for appointment as:

HONORARY PÆDIATRIC PHYSICIAN TO IN-PATIENTS.

Period of appointment: 4 years.

In the event of this position being filled by a present member of the staff, those who have applied for the above position will be considered for the position of Honorary Pædiatric Physician to Out-Patients.

Applications, on prescribed form, close January 30, 1960.

NELL STEPHENSON, Manager.

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OSPITAL APPTS.—Continued

T. VINCENT'S HOSPITAL, SYDNEY.

Applications, closing January 18, 60, are invited for the following acancies on the staff of the new horacic Wing:

MEDICAL REGISTRAR.
SURGICAL REGISTRAR.

Graduates of at least two years' spital experience. Positions are ll-time and live in. Terms of pointment one year, eligible for appointment. Previous experience thoracic work an advantage. It expected duty will commence rly in 1960. Applicants must bmit names of three referees. mmencing gross salary at the te of £1468 to £1943 in accord-ce with experience and qualifi-tions.

THE QUEEN VICTORIA MEMORIAL HOSPITAL, 172 LONSDALE ST., MELBOURNE.

Applications are invited from gally qualified medical women r appointment as:

HONORARY ASSOCIATE OBSTETRICIAN.

Period of appointment: Twelve onths.

Applications, on prescribed form, ose January 30, 1960.

NELL STEPHENSON, Manager.

WAGGA WAGGA BASE HOSPITAL.

MEDICAL SUPERINTENDENT.

Applications are invited from qualified medical practitioners with at least 4 to 5 years experience as Senior Resident Medical Officer or Registrar for the position as Medical Superintendent at the above Hospital. The salary range will be between £2600-£2900 p.a. gross, according to qualifications —as approved by Hospitals Commission of N.S.W.

The successful applicant must be of sufficiently Senior status and capable of not only the duties required of a Senior Resident Medical Officer by the Hospital By-Laws and Rules but also the supervision in its fullest sense of all aspects of the medical work of the hospital, including the control of the admission and discharge of patients.

Applicants should apply in the first instance to the undersigned, stating age, qualifications, past experience and marital status, by Saturday, January 2, 1960.

A. B. SADLEIR.
Chief Executive Officer and Secretary.

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LX 1557 and LX 3778.

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THE COLLEGE OF PATHOLOGISTS OF AUSTRALIA.

EXAMINATION FOR MEMBERSHIP.

Applications to sit for the membership examinations to be conducted during 1960 by the College of Pathologists of Australia should be lodged with the Councillor representing members resident in the State in which the applicant resides. Applications close on February 17 and must be accompanied by the appropriate fee.

Written examinations will be held in June in the capital cities according to the place of residence of applicants. Viva voce examinations will be held in Melbourne in August.

Full details and application forms may be obtained from the Honorary Secretary, 135 Macquarie Street, Sydney.

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